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MEDICAL RESEARCH AND OPERATIONS DIRECTORATE
NASA-MANNED SPACECRAFT CENTER

February 17 and 18, 1966

MANNED SPACECRAFT CENTER
HOUSTON, TEXAS

FOREWORD

This volume constitutes an important segment of the interim reports
of research scientists performing selected investigations under NASA-MSC
contracts or grants. Not all such individuals, to be sure, are herein
represented, since this second annual conference was specifically con-
fined to current studies in the areas of cardiovascular physiology and
neurophysiology. Available results from the biomedical experiments
flown during Project Gemini were also included in these proceedings.
Limitation of the scope of the conference was required in the interest
of time. Future meetings of this kind shall be held on an annual basis
whenever possible, and the reports thereof shall deal with these and
other biomedical or physiological areas germane to the manned space
flight effort.

The Biomedical Research Office wishes to take this means to ack-
nowledge the extraordinary efforts of all the contributors to this vol-
ume whose tireless energies and selfless sacrifice of many precious
hours were required to make the conference such an outstanding success
and to make this report possible.

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MEASUREMENTS OF THE DURATION OF THE CARDIAC CYCLE AND ITS PHASES

IN THE GEMINI ORBITAL FLIGHTS

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SUMMARY

Simultaneous electrocardiographic and phonocardiographic records were obtained from both crew members during the flight of Gemini IV and Gemini V and the pilot of Gemini VII. Analysis of the data recorded during flight reveals wide fluctuations in the duration of the cardiac cycle within physiological limits throughout the mission; fluctuations in the duration of the electromechanical systole that correlated with the changes in heart rate; stable values of the electromechanical delay; higher values of the time of systole and of the electromechanical dalay in the Command Pilot of Gemini V suggesting cholinergic influences; and evidence of adrenergic reaction at lift-off, for several hours after lift-off, at reentry, and for the few hours that preceded reentry. This adrenergic reaction was observed in all the astronauts that participated in this experiment.

OBJECTIVE

The objective of experiment M-4 was to measure the duration of various phases of the electrical and mechanical activity of the cardiac cycle of the astronauts during orbital flights in order to gain information on the cardiac functional status of flight crew members in prolonged space missions.

EQUIPMENT

The experimental equipment system consisted of a phonocardiographic transducer, an electrocardiographic signal conditioner that used a preamplifier and amplifier, and an on-board biomedical tape recorder.

The transducer and signal conditioners were within the Gemini pressure suit. The sensor for the heart sounds was applied parasternally in the left fourth intercostal space of each flight crew member and remained attached to the chest throughout the mission. Electrodes for the detection of the ECG signals were applied in the usual location for the MX lead (manubrium-xiphoid). The phonocardiographic transducer to detect the chest vibrations produced in each heart beat consisted of a 7 mm piezoelectric microphone of 1 inch diameter and 0.2 inch thickness and was developed by the bioinstrumentation section of the Crew Systems Division. A shielded cable 10 inches long connected the heart sounds transducer to the signal conditioner that was located in a pocket of the astronaut's undergarment. The phonocardiographic signal was conducted from the signal conditioner to the suit bioplug and biomedical recorder.

The electrocardiogram and phonocardiogram were recorded simultaneously throughout the flights of Gemini IV and V, and of the pilot in Gemini VII. The recording procedure is entirely passive and does not require active participation on the part of the flight crew members.

ANALYSIS OF DATA

The analog data registered in the biomedical tape recorder were played back in real time after completion of the flight. The records were semiautomatically digitized with a Telecordex analog-to-digital converter. Digital readings were taken at each of the following points: (a) at the onset of QRS complex that marks the beginning of the electrical systole, (b) at the onset of the first heart sound, (c) at the onset of the second heart sound, which indicates the end of the mechanical systole and the beginning of diastole, and (d) at the onset of the next QRS complex, which indicates the end of the cardiac cycle (see fig. 1). A computer program permitted the calculation of the duration of systole and diastole, the interval between the onset of QRS and the first heart sound (electromechanical delay), and the interval between the first and second heart sounds. The same computer program allowed for computation of means and standard deviations of these variables after each 15 consecutive beats (see fig. 2). The regression equation proposed by Hegglin & Holzmann was used to predict the duration of systole for a given heart rate.

Measurements were made in the following periods: (a) continuously starting a few minutes before lift-off and until the spacecraft had reached orbit, (b) continuously from 5 minutes before reentry until splashdown, and (c) continuously for 1 minute at hourly intervals for the first 24 hours of the mission and at 4-hour intervals for the rest of the flight until 5 minutes before reentry.

A   D

O to F =   RR Interval (R)

O to D =   Mechanical Systole
                      plus Excitation Period (S)

PHONOCARDIOGRAM   F – D =   Diastole (D)

O to A =   Q to 1st Sound (T)

O   F   D – A =   1st to 2nd Sound (X)
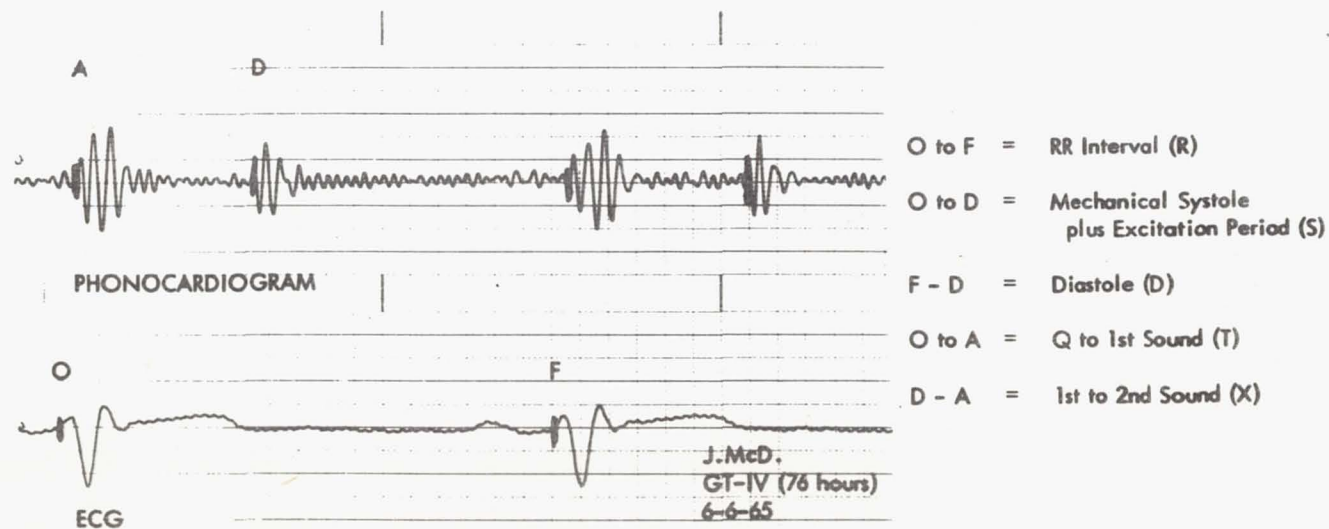
J. McD.
GT-IV (76 hours)
6-6-65

ECG

Figure 1. - Analog record of electrocardiogram and phonocardiogram simultaneously registered. The duration of the cardiac cycle and its various intervals can be derived from digitization of these records at the indicated points.

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192.    -0.    -0.  J. A. MCDIVITT   *********************** J. A. MCDIVITT  GT-4  ***********************     PAGE  1361
                                     70050  /POSIT      1  /TIME    81001  /DATE    60665          CALIB.  31301 .31949

        OBSERVATION   11
            A                                     D                       F
           92.                                  1015.                    2609.

            T           S                        X                                    R          S'
          29.39       324.28                   294.89                               833.55      356.07

        OBSERVATION   12
            A                                     D                       F
           84.                                   983.                    2685.

            T           S                        X                                    R          S'
          26.84       314.06                   287.22                               857.83      361.21

        OBSERVATION   13
            A                                     D                       F
           92.                                  1025.                    2786.

            T           S                        X                                    R          S'
          29.39       327.48                   298.08                               890.10      367.95

        OBSERVATION   14
            A                                     D                       F
           98.                                  1015.                    2687.

            T           S                        X                                    R          S'
          31.31       324.28                   292.97                               858.47      361.35

        OBSERVATION   15
            A                                     D                       F
          137.                                  1004.                    2396.

            T           S                        X                                    R          S'
          43.77       320.77                   277.00                               765.50      341.22
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192.    -0.    -0.  J. A. MCDIVITT   *********************** J. A. MCDIVITT  GT-4  ***********************     PAGE  1362
                                     70050  /POSIT      1  /TIME    81001  /DATE    60665          CALIB.  31301 .31949

        AVERAGE FOR BEAT      1  TO     15


        AVERAGE  T    AVERAGE  S             AVERAGE  X                      AVERAGE  R   AVERAGE S'
          30.33        320.45                 290.12                          843.49       359.14

        STD.DEV. T    STD.DEV. S             STD.DEV. X                      STD.DEV. R   STD.DEV.S'
          4.74          7.32                   9.13                           41.53         8.21

                      RATIO S/S'
                       .892263

                            RANGE OF S            RANGE OF R
                          MIN     MAX           MIN      MAX
              CALCULATED  272.38  368.51       506.10   1180.89
              ACTUAL      301.92  332.27       765.50    897.76
```

Figure 2. - Sample of the computer output of beat-by-beat measurements of the duration of the cardiac cycle and its phases and of averages and standard deviations for 15 consecutive beats.

RESULTS AND DISCUSSION

Similar patterns of change were observed throughout the mission although there were quantitative differences between the individual astronauts.

Figure 3 shows the serial changes in the duration of the total cardiac cycle (line R) of the electromechanical systole (line S), of the electromechanical delay (line T), and of the time interval between the first and the second heart sounds (line X) of the pilot during the flight of Gemini V. The pattern of changes presented here is similar to the patterns observed in all the astronauts who participated in this experiment.

There is usually a marked acceleration of the heart at the time of lift-off. This is reflected in a very short duration of the cardiac cycle accompanied by a proportional shortening in the time of systole and of the electromechanical delay.

There is a gradual deceleration following insertion into orbit but a steady state is not reached until approximately 16 hours from the onset of the mission. Throughout the mission the duration of the cardiac cycle varies considerably with concomitant changes in the duration of the systole and of the time interval between the first and second heart sounds. The electromechanical delay remains relatively constant but usually there is a significant shortening that begins several hours before reentry. In the instance of the pilot of Gemini V, this occurred 20 hours before reentry. Low values of the duration of the cardiac cycle and of its different components are always measured at the time of reentry when peak heart rates ranging from about 160 beats per minute are recorded. It is at this time that the lowest values of duration of the mechanical systole and of the electromechanical delay are recorded.

An interpretation of the significance of these findings requires the establishment of a correlation between the measurements of the time of electromechanical systole, of the electromechanical delay, and the total duration of the cardiac cycle. Figure 4 illustrates this correlation. The average values of the duration of the cardiac cycle corresponding to 15 heart beats at different periods of recording are plotted on the ordinate. The corresponding average values for the electromechanical systole (S), for the electromechanical delay (T), and for the time interval between the first and second heart sounds (X) are plotted along the abscissa. It is clear that the values of S, X, and T are longer when the total duration of the cardiac cycle is also longer (that is, when the heart rate is slower). The normal relationship is shown in the regression line.
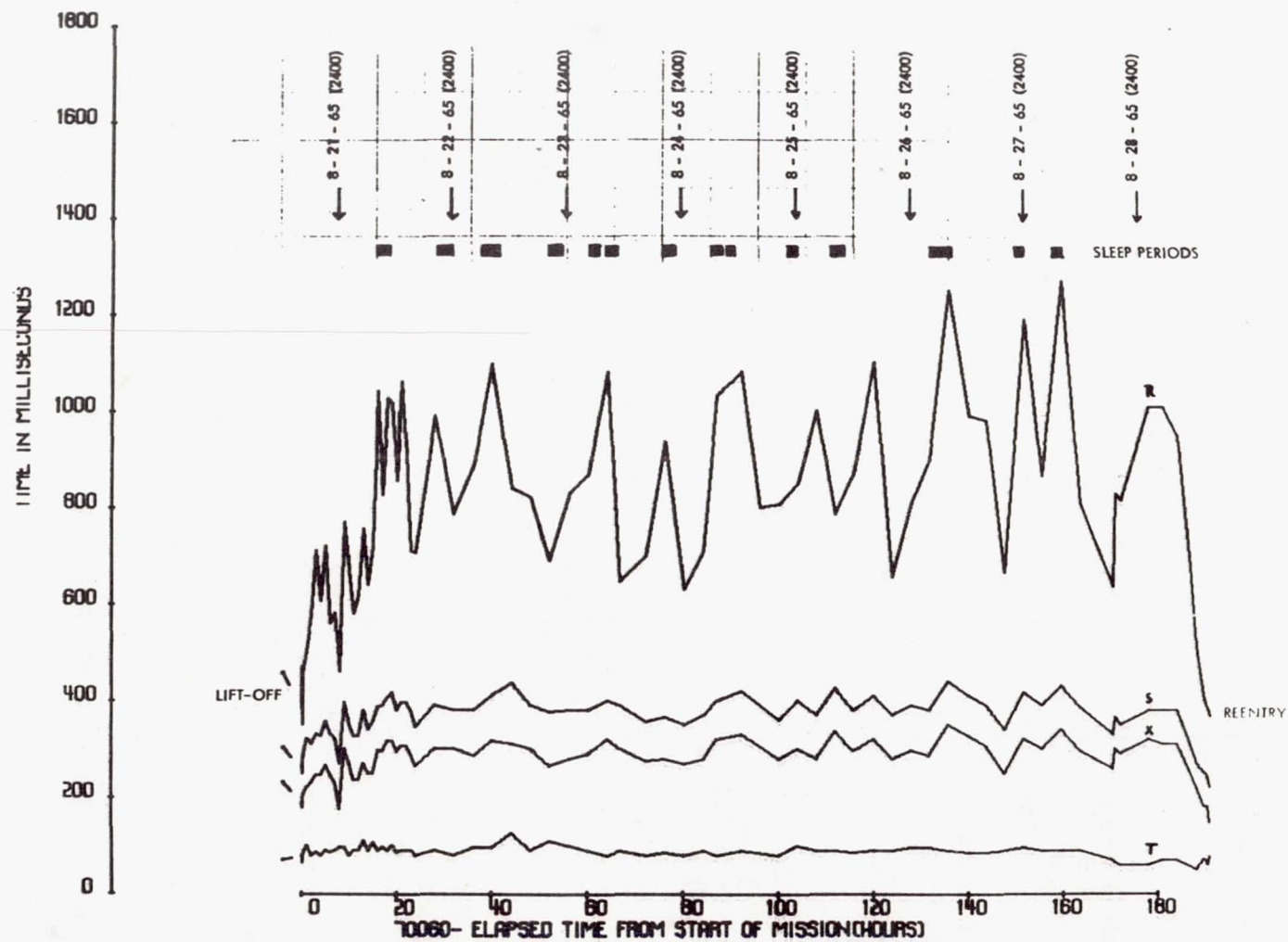
Figure 3. - Serial changes in the duration of the cardiac cycle (R), in the time of electromechanical systole (S), in the interval between first and second heart sounds (X), and in the interval of the electromechanical delay (T) in the Pilot of Gemini V.

Figure 4. - Relationship between the electromechanical systole (S), the time interval between first and second heart sounds (X), the electromechanical delay (T), and the duration of the cardiac cycle (R), throughout the mission of the Pilot of Gemini V.   Each plot represents average values for each period of recording.

In the case of the pilot of Gemini V, these relationships were normal in practically all instances, although values of systole shorter than predicted were measured at the time of reentry. In the case of the command pilot of Gemini IV, and to a lesser extent in the pilot of Gemini IV, the observed values were slightly shorter than normal (see figs. 5 and 6).

Measurements shorter than predicted for a given duration of cardiac cycle are observed under the influence of adrenergic or stress factors while measurements longer than predicted indicate the influence of cholinergic or vagal factors.

A preponderance of adrenergic influences was thus uniformly noticed in all the astronauts at the time of lift-off and, especially, at the time of reentry. This is clearly seen on figure 7 where the values observed at lift-off and before reentry in the pilot of Gemini VII are indicated.

A remarkable quantitative difference was observed in the command pilot of the flight of Gemini V (see fig. 8). His values of systole and of electromechanical delay were significantly longer than predicted for healthy subjects. Only at the time of lift-off and reentry there was a relative shortening of these values. It may be assumed that the longer duration of systole and of the electromechanical delay of the command pilot of Gemini V was an expression of increased vagal tone except at lift-off and reentry. An increased vagal tone was suggested, also, by the marked respiratory sinus arrhythmia, which was recorded in the periods of quietness and sleep.

A prolongation of the electromechanical delay was reported by Baevskii and Gazenko in the flight of cosmonaut Titov. An absolute and relative prolongation of the mechanical systole was reported, also, in the flights of cosmonauts Tereshkova and Bykovskii. It is likely that an increased vagal tone accounted for these observations, but in the case of the command pilot of Gemini V manifestations of nausea or other unwanted signs of vagal preponderance did not occur, we may conclude that the finding of a prolonged electromechanical delay does not have in itself a pathological significance.
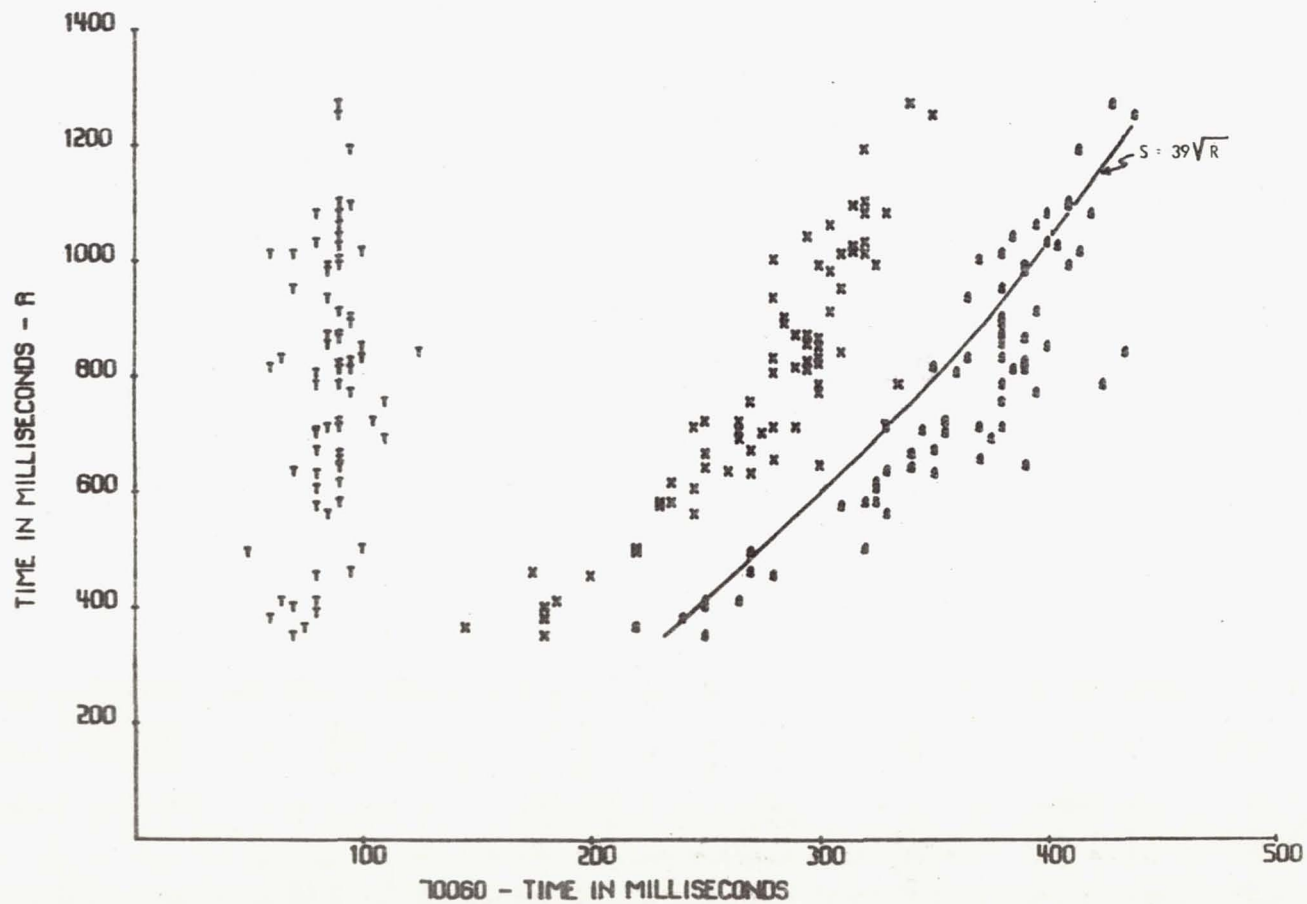
Figure 5. - Relationship between the electromechanical systole (S), the time interval between first and second heart sounds (X), the electromechanical delay (T), and the duration of the cardiac cycle (R), throughout the mission of the Command Pilot of Gemini IV. Each plot represents average values for each period of recording.
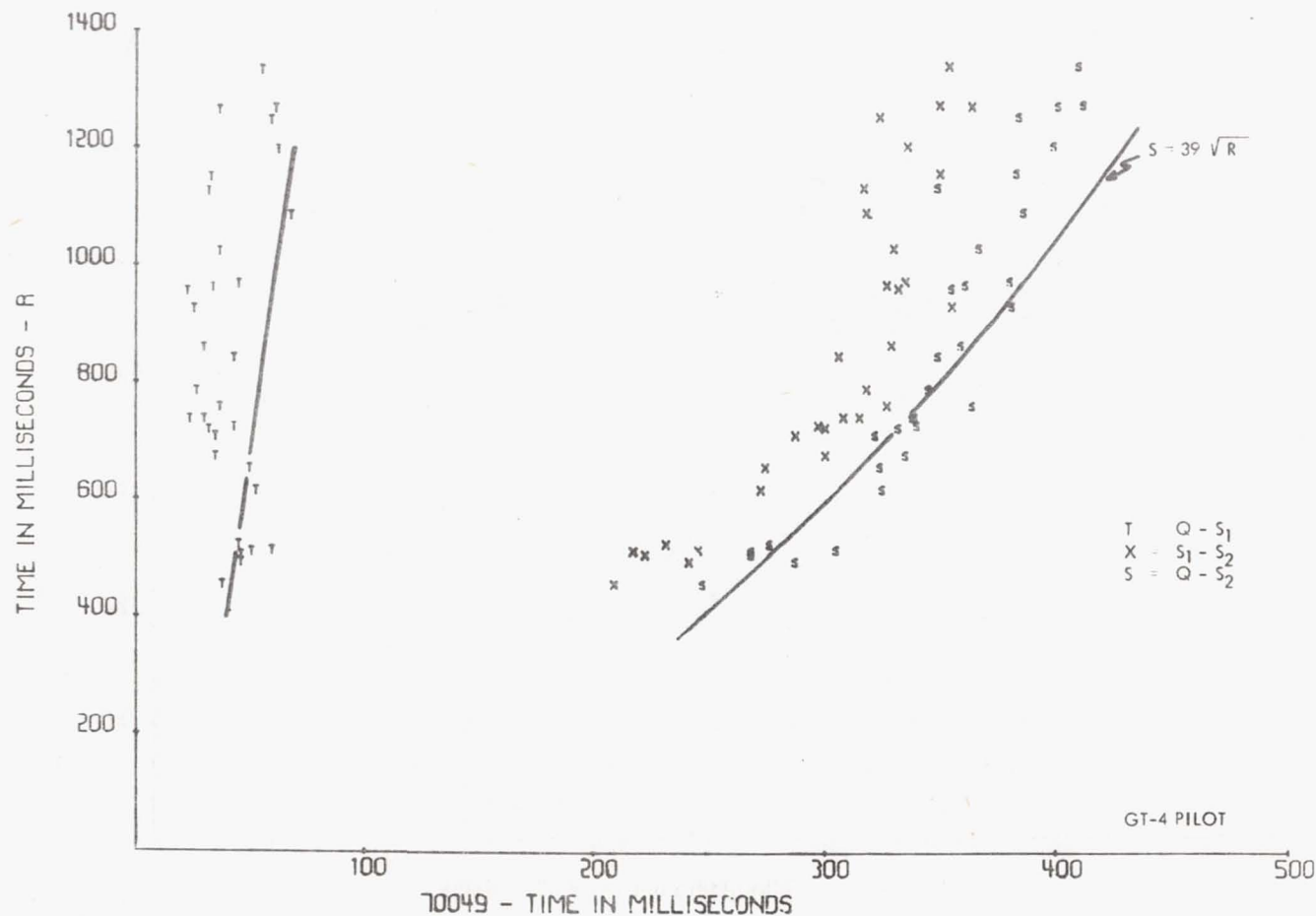
Figure 6. - Relationship between the electromechanical systole (S), the time interval between first and second heart sounds (X), the electromechanical delay (T), and the duration of the cardiac cycle (R), throughout the mission of the Pilot of Gemini IV. Each plot represents average values for each period of recording.
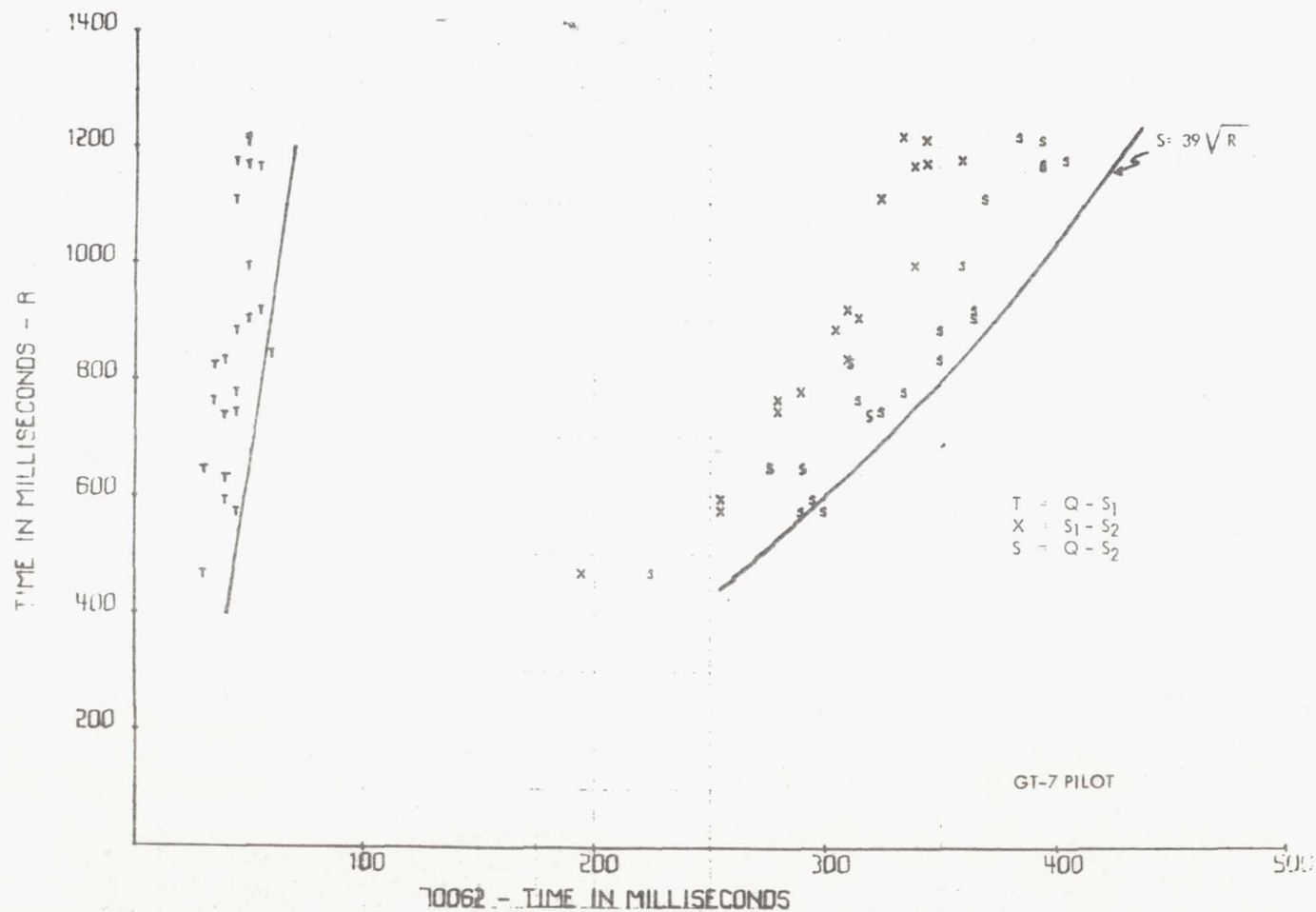
Figure 7. - Relationship between the electromechanical systole (S), the time interval between first and second heart sounds (X), the electromechanical delay (T), and the duration of the cardiac cycle (R), throughout the mission of the Pilot of Gemini VII. Each plot represents average values for each period of recording. The values shown in this graph include only values obtained at lift-off and at reentry.
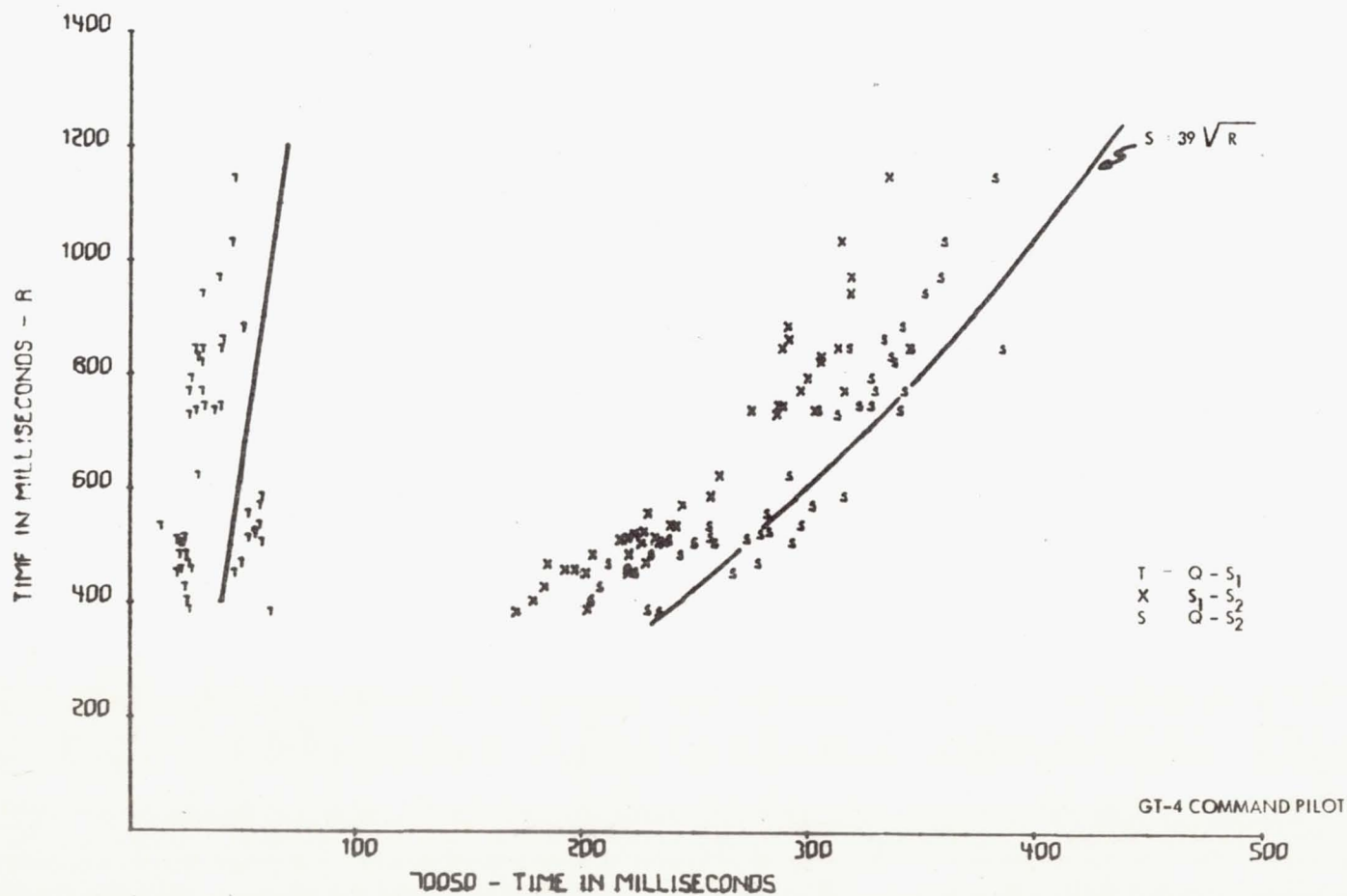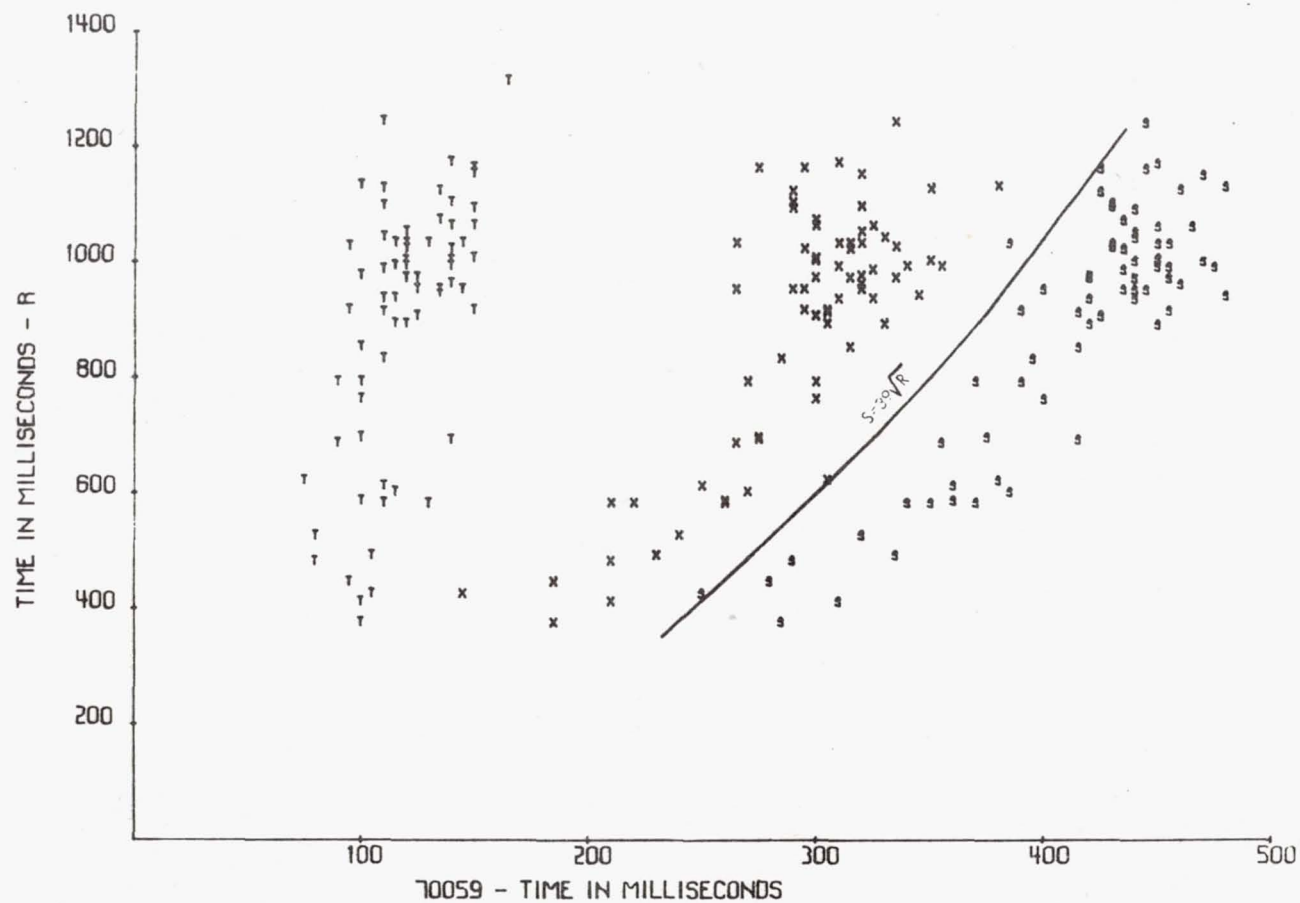
Figure 8. - Relationship between the electromechanical systole (S), the time interval between first and second heart sounds (X), the electromechanical delay (T), and the duration of the cardiac cycle (R), throughout the mission of the Pilot of Gemini V. Each plot represents average values for each period of recording.

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PLASMA VOLUME AND EXTRACELLULAR FLUID VOLUME CHANGE

ASSOCIATED WITH TEN DAYS BED RECUMBENCY

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A decrease in plasma volume has been noted to occur during various ground-based deconditioning experiments, as well as in association with recent Gemini space flights. Some investigators have speculated that a decrease in plasma volume is one of the primary mechanisms responsible for the manifestations of tilt table intolerance seen after such deconditioning experiments. Supportive evidence for this hypothesis has resulted from tilt table studies performed after rapid removal of known amounts of blood from individuals, thus eliminating certain components of cardiovascular deconditioning, such as physical inactivity, but at the same time possibly introducing other unknown reflex mechanisms. It also has been speculated that this decline in plasma volume is associated with a corresponding decline in extracellular fluid volume, especially in the lower portions of the body. The proposed mechanism responsible for the decline in the volume of these spaces involves a physiological adaptation of the body from the condition wherein there are relatively large hydrostatic pressure forces at the capillary level that occurs periodically in persons undergoing normal activity, to the condition where these forces are removed when there is a lack of gravity acting parallel to the long axis of the body.

It is the purpose of this paper to document the changes in the plasma volume and extracellular fluid compartments, and other related measurements during three periods of 10 days recumbency in a group of 10 subjects. The experimental design utilizes potential treatment measures which could be used in an actual flight situation. The design does not allow direct correlation between the decline in plasma volume and tilt table intolerance observed in these subjects and as reported elsewhere. This paper is one of a series of reports which describe in detail the changes in various tests performed and measurements made on a group of subjects participating in a complex experimental design.

METHOD

Subjects

Eleven healthy adult young male subjects participated in three periods of 10 days bedrest conducted at the Texas Institute for Rehabilitation and Research in the summer of 1964. Subject characteristics are shown in table I. Subject A.P.K. participated in the first period of recumbency only, and was replaced by L.F.E. who participated in the remaining two periods of recumbency. Subjects who actively engaged in competitive sports and followed a regular physical training schedule were classified as athletes.

Calendar of Experimentation

The calendar of experimentation is shown on figure 1. The subjects were divided into two groups for convenience in testing, with one-half of the subjects going into bedrest a day before the other half. Similarly, the first group of subjects was ambulated 1 day earlier than the second group. During the first recumbency period, subjects M.A.C., R.S.H., J.A.H., G.S.R., and B.E.H. had intermittent leg cuff inflation, while the remainder of the subjects underwent a periodic exercise program. Finally, during the third period of recumbency, all subjects went through a 10-day period of bedrest without any potentially protective mechanisms.

Experimental Circumstances

The subjects were admitted to the Texas Institute for Rehabilitation and Research as patients for experimental studies. During a 94-day stay at the hospital, they were fed controlled diets containing approximately 8 to 10 grams of salt daily. Fluid intake was allowed ad libitum. In the intervals between bedrest periods, the subjects were maintained on controlled diets and sleep schedules. During the day, they were encouraged to follow activity patterns similar to that followed prior to admission, except for the imposition of food and sleep control. During the periods of recumbency, the subjects were required to maintain a horizontal position in bed. They were allowed one pillow under their heads, were allowed to roll from side to side in bed, and by turning on their sides, were allowed to feed themselves. The subjects were under supervision of a physician at all times during recumbency.

TABLE I

Subject Characteristics

Subject Initials	Hospital Number	Age (yrs.)	Weight* (kg.)	Height* (cm.)	BSA** (m.^{2})	Occupation
M.A.C.	70020	23	65.3	177.8	1.81	Student(NA)
L.F.E.****	70028	24	74.3	188.0	2.00	Student(A)
R.S.H.	70021	22	65.2	172.4	1.77	Student(A)
J.A.H.	70022	23	81.1	179.0	2.01	Student(NA)
B.E.H.	70019	21	69.8	177.8	1.88	Student(NA)
A.C.I.	70018	22	51.0	163.0	1.52	Student(A)
A.P.K.***	70023	24	59.4	174.0	1.72	Student(NA)
W.F.M.	70024	23	66.4	171.0	1.78	Student(NA)
C.E.R.	70025	25	80.6	192.4	2.11	Student(A)
G.S.R.	70026	26	65.6	177.8	1.83	Student(A)
R.R.T.	70027	22	78.2	172.4	1.92	Student(NA)

   A   Athlete
 NA   Non-athlete
   *   At the beginning of the experiment
  **   Dubois Body Surface Chart (prepared by Boothby and Sandiford)
 *** Participated only in the first period of bedrest
**** Participated only in the second and third periods of bedrest

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CALENDAR OF EXPERIMENTATION						
S	M	T	W	T	F	S

JUNE

| | | 1 | 2 | 3 | 4 | 5 | 6 |

| 7 | 8 | 9 | 10 | 11 | 12 | 13 |

| 14 | 15 | 16 | 17 | 18 | 19 | 20 |

| 21 | 22 | 23 | 24 | 25 | 26 | 27 | RECUMBENCY PERIOD NO. 1

| 28 | 29 | 30 | 1 | 2 | 3 | 4 |

JULY

| 5 | 6 | 7 | 8 | 9 | 10 | 11 |

| 12 | 13 | 14 | 15 | 16 | 17 | 18 |

| 19 | 20 | 21 | 22 | 23 | 24 | 25 |

| 26 | 27 | 28 | 29 | 30 | 31 | 1 | RECUMBENCY PERIOD NO. 2

AUGUST

| 2 | 3 | 4 | 5 | 6 | 7 | 8 |

| 9 | 10 | 11 | 12 | 13 | 14 | 15 |

| 16 | 17 | 18 | 19 | 20 | 21 | 22 |

| 23 | 24 | 25 | 26 | 27 | 28 | 29 |

| 30 | 31 | 1 | 2 | 3 | 4 | 5 | RECUMBENCY PERIOD NO. 3

SEPTEMBER

| 6 | 7 | 8 | 9 | 10 | 11 | 12 |

TILT   PRE-RECUMBENCY OBSERVATION
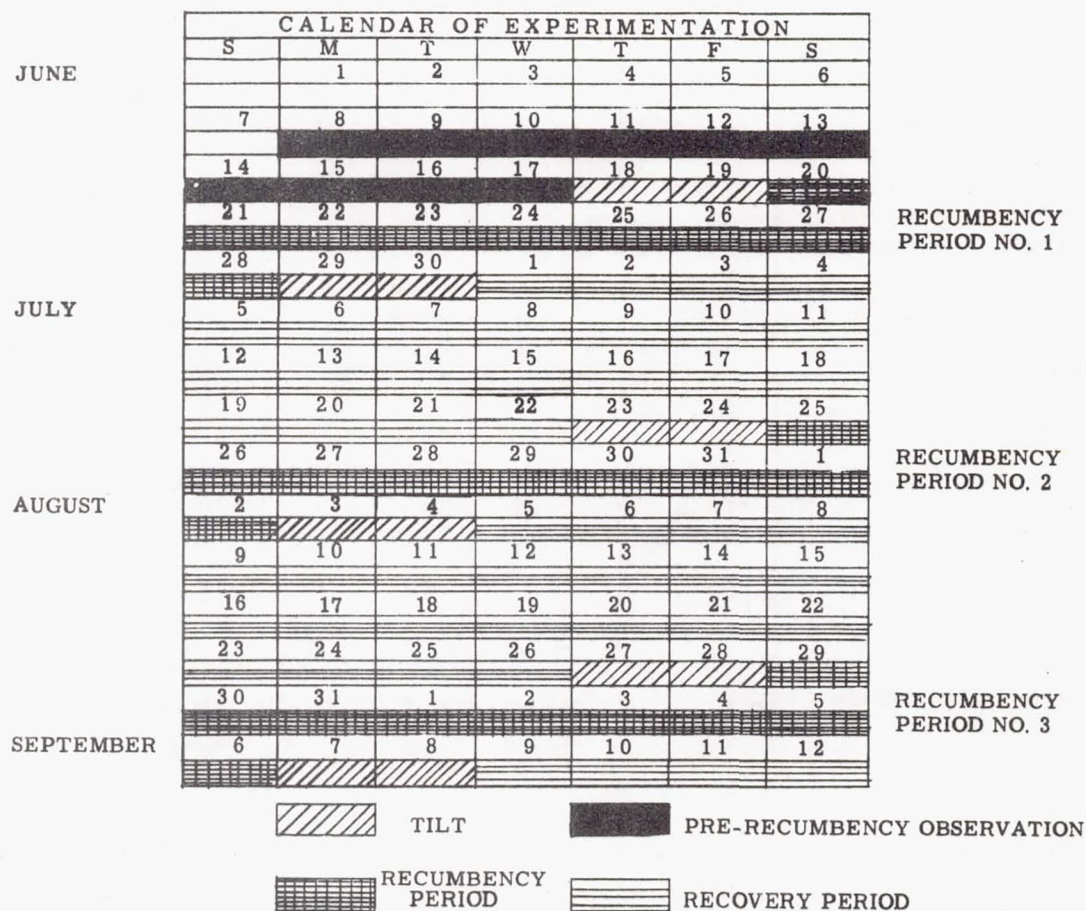
RECUMBENCY PERIOD   RECOVERY PERIOD

Figure 1. - Calendar of experimentation.

Cuff treatment was provided 24 hours a day during the 10-day period of recumbency, using 3.75-inch-wide cuffs applied to the upper part of the thigh, inflated to a pressure of 70 to 75 mm Hg. The cuff inflation-deflation cycle was 5 minutes on and 10 minutes off, with the cuff inflation phase taking 5 to 8 seconds. Bungie-cord exercises were provided hourly for 10 treatment periods a day, starting at 8:00 a.m. The exercises were performed in the horizontal position by the subject placing his feet in a bracket at one end of the rubber Bungie cord to provide a fixed point against which to pull. The subject kept his legs partially flexed to provide muscular exercise to the lower as well as the upper extremities. The extent or length of pull attained for each Bungie-cord exerciser was determined for each subject prior to bedrest. For each subject, a work load was determined which produced a moderate cardioacceleration in response to the exercise, which consisted of 120 pulls on a prescribed exerciser at a rate of one pull per second.

Body compartment measurements were performed periodically during the 94-day experiment using a multiple isotope dilution technique.[1] Primary attention was directed at evaluation of plasma volume and extracellular fluid volume changes, although periodic red cell mass and total body water determinations were done as described in Tests Performed. A Packard Autogamma System was utilized for determination of iodine $\left(I^{131} \text{ and } I^{125} \right)$ and chromium $\left(Cr^{51} \right)$.

Tests Performed

Plasma volume (PV) was determined using iodinated human serum albumin (IHSA), allowing a mixing time of 10 minutes. Measurements were made in the control period prior to and after recumbency, on the first day of recumbency (after the subjects had been horizontal for approximately 12 hours) and on days 4 and 10 during the recumbency period. Determinations made during the ambulatory periods were obtained within 2 hours of the time the subjects arose after a night's sleep. Duplicate 1-ml samples of plasma were counted on the Packard Autogamma. Injected doses of IHSA were increased during the course of the experiment, as required to obtain valid results considering injections of isotope from previous tests.

Extracellular fluid volume (ECF) was determined by using the sodium sulfate $\left(S^{35} \right)$ dilution technique. Venous blood samples were withdrawn at 60, 120, 150, and 180 minutes after injection of the

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[1]The detailed technique is available upon request from the authors.

isotope for construction of a dilution curve used in calculating the extracellular fluid volume.

Red blood cell mass was determined several times prior to the first period of recumbency by a technique using sodium chromate (Cr^{51}) tagged red blood cells. A 10-minute mixing period was allowed after injection of the tagged cells before the determination. These prerecumbency tests served as baseline determinations for comparisons to a single red cell mass determination made after the second period of recumbency. More frequent measurements of red cell mass were not made because of the isotope dose exposure required in these extensive studies performed repeatedly on the same subjects.

Total body water (TBW) determinations, utilizing a tritiated water dilution technique, were done on days 1, 4, and 10 of recumbency periods one and three, as well as several times prior to recumbency period one, and once in the interim between periods two and three. More frequent measurements were not made because of the cumulative dose of isotope, which would have been required to obtain technically acceptable results. Venous blood samples were withdrawn at 60, 120, 150, and 180 minutes after injection of the radioactive water dose to determine the dilution curve for calculation of the total body water volume.

Hematocrits (Hct.) were determined using a microcapillary technique and centrifuging the venous blood for 5 minutes. Prior to breakfast, and after urination, body weights were determined on a platform scale which could be read to ±50 grams. Circumference measurements were made daily at three sites on each leg during the course of the study; changes in calf circumference during tilt were measured during tilt procedures, using a mercury-in-rubber strain gauge apparatus.

Data Analysis

Data were analyzed using a least squares analysis of variance technique. The results presented here refer to the nine subjects who participated in all three periods of recumbency. The analysis of variance technique utilized three main effects of treatment, day, and athlete/nonathlete subject classification, with use of interactions between the three to arrive at the residual term for calculating the F values presented in the tables. In table II is shown an example of a computer printout of the analysis of variance performed, with a printout of a table of means tabulated below the results of the analysis of variance. For simplicity of discussion, the data collected on days 1, 4, and 10 of bedrest are considered in more detail than other data collected during the control periods.

TABLE II

Sample Analysis of Variance Performed on Data

Day (1, 4, 10)		Analysis of Variance		E.C.F.
	DF	SS	MS	F
Total	80.	0.497222900E 03		
Athlete/Non-athlete	1.	0.180500799E 02	0.180500799E 02	3.0578
Treatment	2.	0.330019508E 01	0.165009756E 01	0.2795
Day	2.	0.656642903E 02	0.328321454E 02	5.5620
Interaction	2.	0.700192451E 01	0.350096226E 01	0.5931
Interaction	2.	0.727037741E 01	0.363518870E 01	0.0062
Interaction	4.	0.736740553E 01	0.184185135E 01	0.3120
Residual	67.	0.395495360E 03	0.590291583E 01	

Table of Means for Main Effects

Athlete/Non-athlete	14.6611	15.6111	
Sample Size	36	45	
Treatment	15.4296	15.0667	15.0704
Sample Size	27	27	27
Day	16.3000	15.1926	14.0741
Sample Size	27	27	27

RESULTS

In table III is presented an overall summary of F values for the analysis of variance performed on the measurements obtained for plasma volumes, hematocrit, total body water, and extracellular fluid. Since there was no statistical significance (at $p = 0.05$) in the analysis of variance for the main effect, treatment, the results of the treatments of bedrest, bedrest with cuffs, and bedrest with exercise will be discussed as representing statistically the same experimental condition, describing primarily the effects from recumbency. There is noted in table III highly significant differences in athlete and nonathlete for the measurements plasma volume and hematocrit. An analysis of variance performed using the main effect, day of treatment, indicates significant changes in plasma volume, hematocrit, and extracellular fluid volume. Interaction between the main effects were statistically non-significant in this experiment.

In table IV is summarized the means for the three treatment periods of the measurements made on days 1, 4, and 10. The following figures display the means obtained for the various measurements on different treatment days. On figure 2 is shown the average plasma volume change by day for the three periods of recumbency. On figure 3 is shown the corresponding hematocrit changes for the same day, indicating the inverse relationship between these two measurements. The average extra-cellular fluid volume changes by day for the bedrest periods combined is shown on figure 4, indicating a continuous trend downward in this measurement. On figure 5 the average total body water volumes by day for periods one and three combined are presented. In table V is presented the comparison for athletes and nonathletes for all measurements combined.

There was an average decline in red cell mass of 215, comparing the prerecumbency value of 2265 ml for the nine subjects with the 2050 ml value obtained midway between the second and third periods of recumbency. There was a variable change in body weight after the periods of recumbency, with small increase or decrease in different subjects; no consistent pattern of weight change was observed.

Leg circumference changes, measured at the calf, showed a small but indefinite decrease during the periods of recumbency, with no increase in circumference noted in the subjects when cuff treatment was in operation. No definite correlation could be established with tilt intolerance and the amount of decrease in plasma volume.

TABLE III

Over-all Summary of F Values

Subject	Day	Ath./Non-Ath.	Treatment	Day	I_{12}	I_{13}	I_{23}
P. V.	1, 4, 10	4.89*	1.15NS	7.17**	0.00NS	0.22NS	0.58NS
H. C. T.	1, 4, 10	41.30**	2.35NS	32.31**	2.90NS	0.12NS	0.77NS
T. B. W.	1, 4, 10	0.35NS	0.89NS	0.45NS	0.06NS	0.22NS	1.35NS
E. C. F.	1, 4, 10	3.06NS	0.28NS	5.56**	0.59NS	0.01NS	0.31NS
P. V.	1, 4	4.80*	1.70NS	8.21**	0.00NS	0.11NS	0.20NS
H. C. T.	1, 4	24.06**	0.97NS	45.05**	1.93NS	0.08NS	1.11NS
T. B. W.	1, 4	0.56NS	0.00NS	0.10NS	0.02NS	0.08NS	1.05NS
E. C. F.	1, 4	1.89NS	0.22NS	2.43NS	0.55NS	0.01NS	0.54NS

$$* \quad p < 0.05$$
$$** \quad p < 0.01$$
$$NS \quad \text{non-significant}$$

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TABLE IV

Average Values for Bedrest Days for
Three Treatment Periods Combined

Measurement	Day 1	Day 4	Day 10
Plasma Volume (liters)	3387	3055	2963
Hematocrit (%)	41.1	45.0	44.3
Total Body Water (liters)	45.8	45.1	45.1
Extracellular Fluid (liters)	16.3	15.2	14.1

TABLE V

ATHLETE/NON-ATHLETE COMPARISONS

(Average of All Determinations)

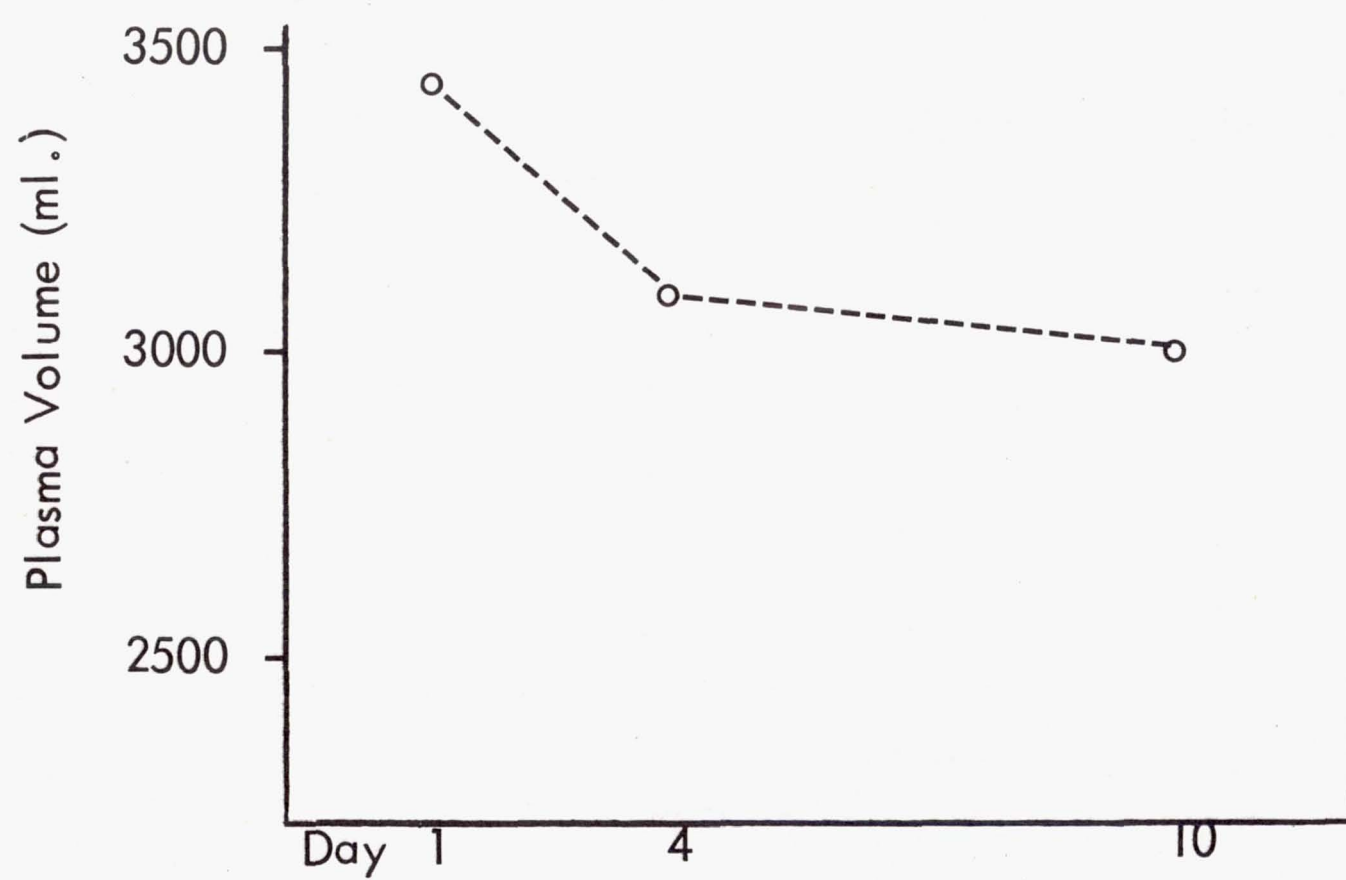|	Athlete	p	Non-Athlete
Plasma Volume (ml.)	3256	0.03	3039
Hematocrit (%)	44.7	< 0.001	42.0
Total Body Water (liters)	45.8	0.56	45.0
Extracellular Fluid (liters)	14.7	0.08	15.6

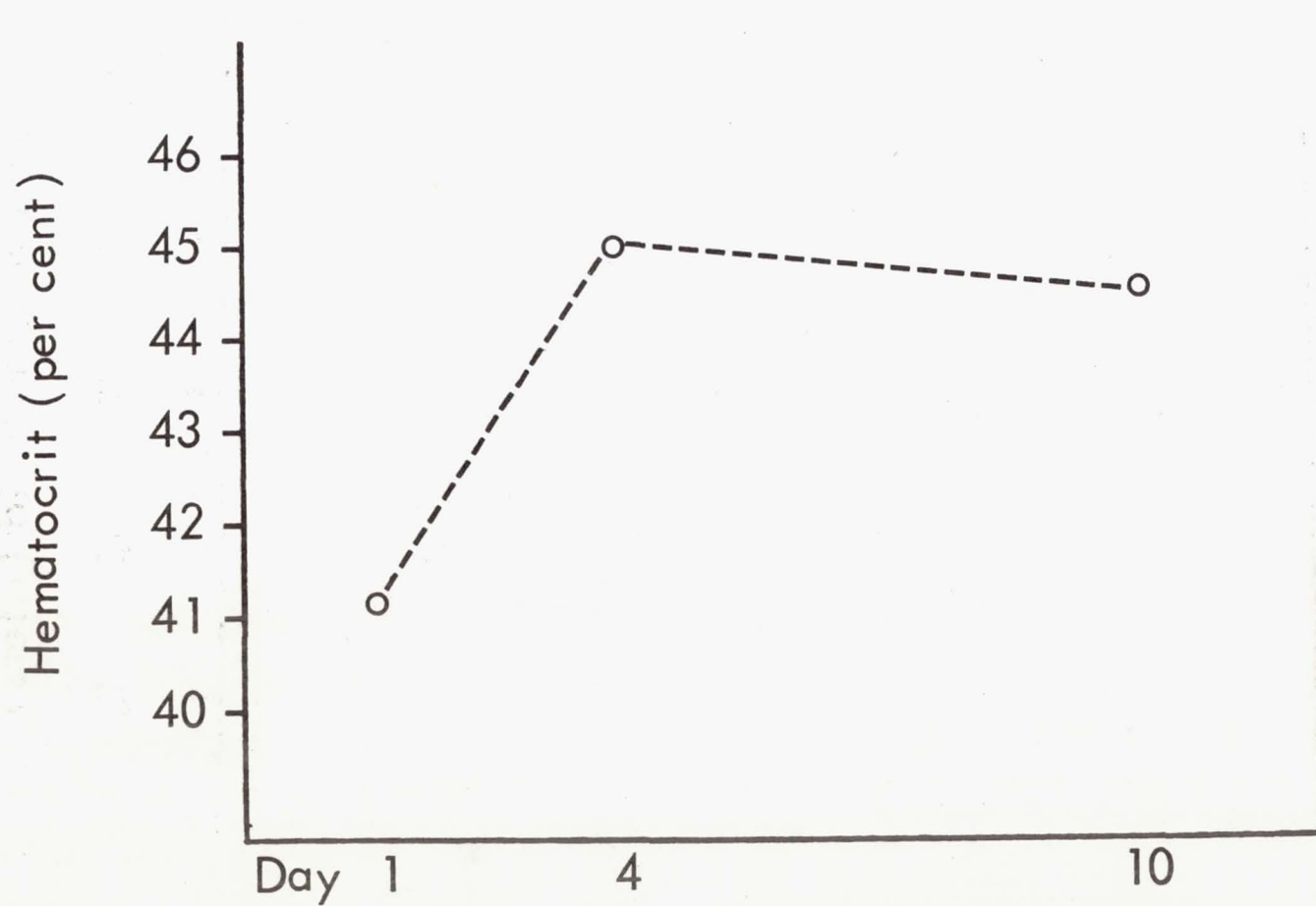Figure 2.- Average plasma volumes of bedrest days of three treatment periods combined.

Figure 3. - Average hematocrit for bedrest days of three treatment periods combined.
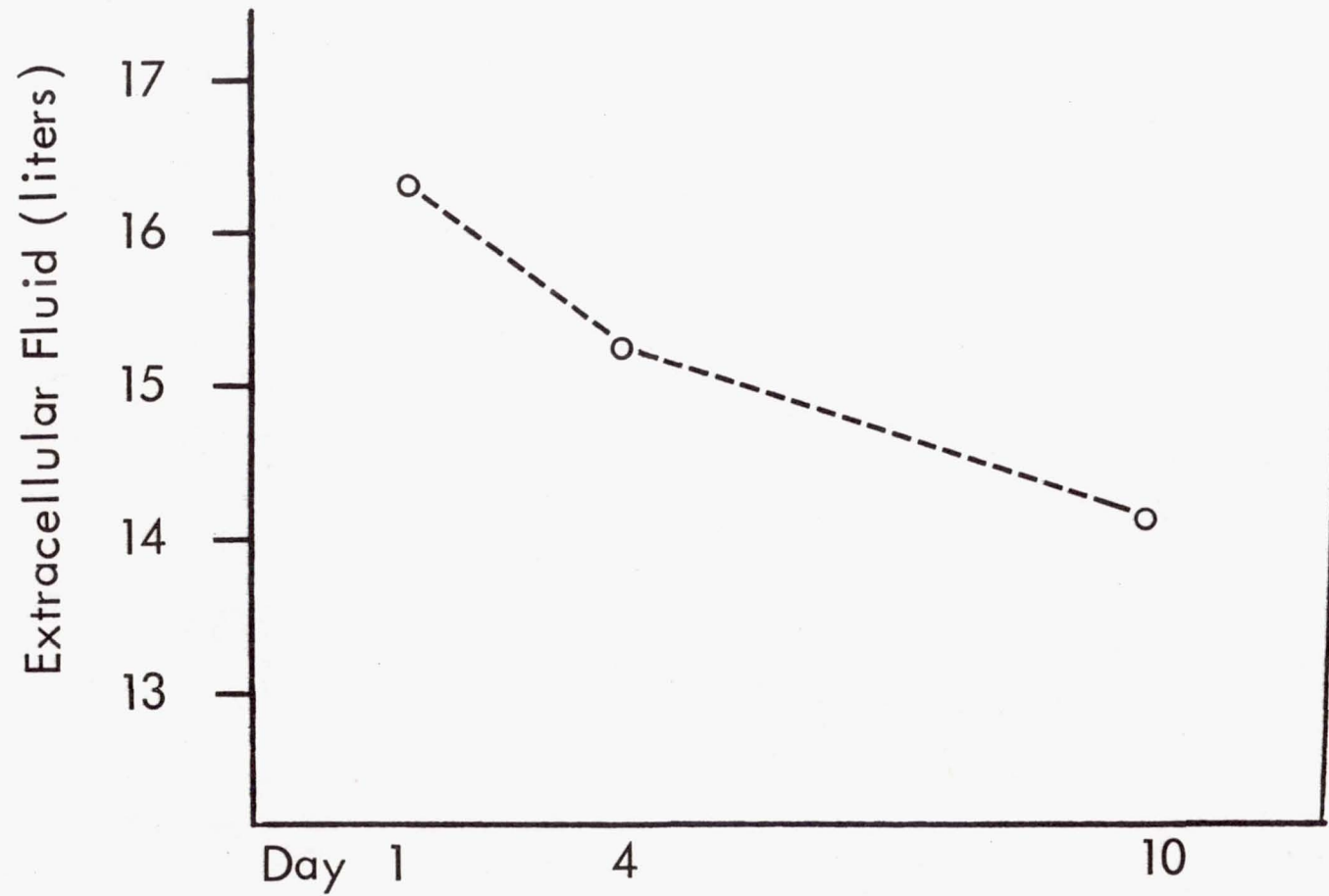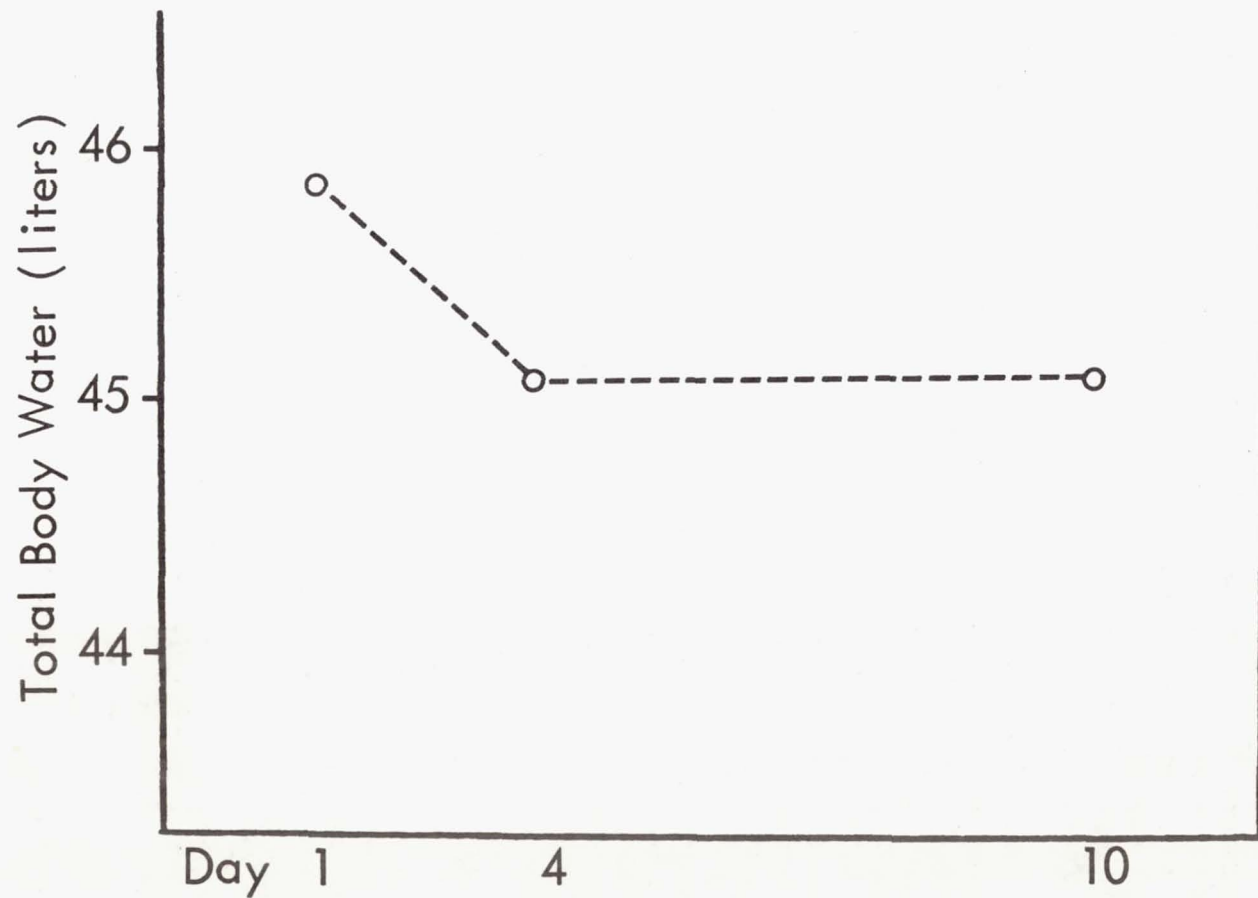
Figure 4.- Average extracellular fluid for bedrest days of the three treatments combined.

Figure 5. - Average total body water for bedrest days of periods one and three combined.

DISCUSSION

The observation of no statistically significant differences in the group response for the treatments used in this experiment does not necessarily mean that no effect results from the treatments; more exercise or different cuff timing cycles may have produced significantly different results. Treatment measures were devised and tested experimentally using an experimental design that could be applied to a space flight situation.

The rapid decline in plasma volume showed a stabilization in volume between days 4 and 10. Some studies provide evidence that this decline reverses as the deconditioning period progresses, while other investigators have noted large changes in plasma volume or blood volume associated with prolonged recumbency. Other work conducted by the authors in similarly controlled experimental circumstances would support the first observation. Observation of tilt table intolerance after prolonged recumbency, with corresponding return of blood volume to normal values, suggests that though decrease in plasma volume could be one factor responsible for tilt table intolerance, it is not the only mechanism operating to produce the effect. From the authors' observations, it would be concluded that under controlled experimental circumstances, it is likely that vascular volume compensatory mechanisms will result in a restoration of "normal" blood volumes as the experiment progresses.

In contrast, the data from this study indicates a progressive decline in extracellular fluid volume. No further data are available to predict whether this decline is likely to progress for a longer period of time. This decline in extracellular fluid volume could be a contributing mechanism to the tilt intolerance seen after deconditioning, if there results an increased transudation of fluid from the vascular to extravascular space when the subject is exposed to gravity vectors acting parallel to the axis of his body during the tilt procedure after deconditioning.

The failure to observe statistically significant changes in total body water is accompanied by failure to observe weight changes of the subjects. The sensitivity of the method to determine total body water may not be great enough to detect the changes which could be expected under these experimental circumstances. No further interpretation of these measurements is thought justified from the present experimental design.

The decline in red cell mass is probably a real accompaniment of the experimental procedure (bedrest), although repeated removal of

blood for laboratory testing must be considered as potentially affecting this measure, especially in view of the small change observed in red cell mass. The exact relation of the measurement to the periods of recumbency cannot be ascertained, as values were obtained prior to recumbency and between the second and third periods.

The use of the day 1 value as the control value for the measurement was selected by the authors because the subjects had been in bed only 12 hours, which would correspond closely to performing measurements on subjects early in the morning on other so-called controlled days. These measurements were not significantly different from the prerecumbency measurements and those obtained on day 1 of the first period after 12 hours recumbency. There could be a small bias toward an increased plasma volume after short periods of recumbency, as has been described for certain patients, but which has not been documented clearly in normal subjects.

These data, collected under controlled experimental circumstances, show the reproducibility of the technique and the apparent validity of the methodology for studies of this type. Further documentation of the transistory or progressive changes in the observed measurements must be made before they can be related to tilt table tests as mechanisms of tilt intolerance or simply as occurring incidentally because of the temporal relation of the test procedures.

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RED CELL MASS AND PLASMA VOLUME CHANGES OF SPACE FLIGHT

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With each passing year, radioisotope techniques become more important in biological research and clinical medicine. With the flight of Gemini IV, medical radioisotope investigations were extended, for the first time, into the realm of near space. The radioisotope studies that started with Gemini IV have subsequently proven to be an efficacious means of studying various aspects of man's response to this new environment. To date, the human radioisotope studies performed for the Gemini program have included plasma volumes, red cell masses, and red cell survivals.

Physiological investigations following the early Gemini and Mercury flights showed alterations in response to a passive tilt which were qualitatively similar to the changes found after bed rest. Ground-based bed rest and water immersion studies have shown that intolerance to passive tilt is associated with a spectrum of altered cardiovascular responses, which includes changes of plasma volume. The initial radio-isotope studies performed on the Gemini IV astronauts showed decreases in plasma volume similar to the decreases discovered during the bed rest studies of similar duration. These studies, using iodinated human serum albumin I^{125}, were performed 2 days before launch and immediately after recovery. Calculation of blood volume and red cell mass, derived from the venous hematocrit and plasma volume data, showed decreases in both parameters after flight. Because calculation of blood volume from plasma volume and peripheral hematocrit values may give incorrect results, it was deemed advisable to include direct Cr^{51} red cell mass determinations for both Gemini V and VII. The inaccuracy of indirectly derived blood volumes eminates from significant and unpredictable changes in the ratio of total body to peripheral hematocrit.

The results of all radioisotope determinations performed on the crews of Gemini IV, V, and VII will be described. These preliminary studies of space flight physiology showed variable changes in the plasma

volume and a consistent decrease in the red cell mass of the returning astronauts.

METHODS

All determinations of plasma volume and red cell mass were preceded by a 15-minute recumbent interval. Background blood samples were obtained prior to each radioisotope series to correct for any previously injected radioactivity. All plasma volume measurements were accomplished with iodinated human serum albumin tagged with I^{125}. The radioactive albumin was diluted with normal saline to a concentration of 0.4 microcuries/ml preflight and 0.8 microcuries/ml postflight and placed in multiinjection bottles. Carrier human serum albumin was added to the diluted radioactive albumin to inhibit radiation denaturization prior to injection. For all preflight plasma volume determinations 2 microcuries of I^{125}, as iodinated human serum albumin, were injected whereas postflight 5 microcuries were used. Fifteen minutes equilibration times were adhered to throughout the series. All blood was drawn from antecubital veins into heparinized syringes. The whole blood samples were then centrifuged, the plasma removed, and two 1-ml aliquots from each sample pipetted into counting tubes. Standards were prepared by diluting 2 or 5 microcuries of radioactive albumin in 1 liter of tap water. Nonradioactive albumin had been previously added to each standard, liter, volumetric flask to prevent absorption of the radioisotope by the glass. The standard aliquots were immediately pipetted for subsequent counting. All I.V. injections were made using disposable plastic syringes, and the same type of syringe was used in preparing all standards. Nearly all residual radioactivity in the dose syringes was removed by irrigating them with 2 ml of water which was then counted. The infinite, total body radiation exposure per astronaut, for the entire plasma volume series, was approximately 2.5 mrem.

The red cell mass determinations were performed by adding a 15-ml aliquot of the astronaut's blood to 5 ml of ACD solution contained in a Unitag Bag[1]. To this solution, 100 microcuries of sodium chromate (Cr^{51}) were added. After an incubation period of 10 to 12 minutes at room temperature, 100 mg of ascorbic acid were injected into the bag to terminate the tagging process. After thorough mixing, a 10-ml aliquot of the incubate was reinjected into the astronaut from whom the blood had been drawn. The remaining incubate was retained for the preparation

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[1]Abbott Laboratories

of standards. A venous blood sample was obtained after allowing an in-
vivo mixing time of exactly 15 minutes from which a hematocrit was ob-
tained and duplicate aliquots of whole blood and plasma were submitted
for radioisotope determination. The blood remaining in the Unitag Bag
was used for determining the incubate hematocrit and pipetting duplicate
1-ml aliquots into counting tubes. The remainder of the incubate was
then centrifuged, the plasma removed, and two 1-ml aliquots of the
plasma pipetted into counting tubes.

The erythrocyte survival half-times were measured from the disap-
pearance of chromium-tagged red cells and were corrected for changes
in red cell mass. A sample obtained 24 hours after the injection of the
radioactive cells was used as the zero time for each survival determina-
tion. This prolonged mixing time was used to allow removal of cells
inadvertently injured during the tagging procedure. The total radiation
dose delivered per astronaut, for the entire Cr^{51} red blood cell mass
determination series, was about 84.8 mrem.

All samples were counted in an automatic scintillation well detector
using a pulse height analyzing scaler to separate the energy peaks of
I^{125} (0.035 - 0.0275) from that of Cr^{51} (0.323). Sufficient counts were
collected to reduce the counting error to less than 0.5 percent. The
formulas used for all calculation can be found in the appendix. For
each astronaut, the predicted normal red cell mass and plasma volume
were derived from the nomogram of Hidalgo et al., for I^{131} human serum
albumin blood volume (B.V.). Preflight weights and heights were used
in determining the blood volumes from the nomogram.

RESULTS

Table I shows the results of the red cell mass determinations ob-
tained from Gemini IV, V, and VII pilots. The predicted normal red cell
masses of four of the astronauts compared favorably to their preflight
measurements; however, the red cell mass of the Gemini IV pilot was
752 ml greater than his estimated normal and the Gemini VII pilot had an
initial red cell mass which was 178 ml less than his estimated normal.
Postflight, all pilots showed a decrease in their red cell mass ranging
from 144 ml to 441 ml. Also shown are the red cell masses that were
determined 18 or 20 days after the return of the Gemini VII crew.
Gemini VII was the only flight for which a determination was made nearly
3 weeks after recovery. In this flight, red cell masses had returned
to essentially preflight values by that time. Because the red cell
masses shown for Gemini IV were not determined directly, but were de-
rived from plasma volume determinations, the differences in the pre-
flight and postflight red cell mass values are correct only if the

ratio between the venous hematocrit and total body hematocrit remained identical in these two situations. Good evidence, derived from subsequent missions, indicates that this assumption is not correct.

Table II shows the results of the Cr^{51} red cell half-time determinations. During the Gemini V mission, the red cell half-times of both astronauts were below our normal range. Similar results were seen in the command pilot (CP) of Gemini VII but were not seen in the pilot (P) of that mission. This crewman represents the only anomaly with respect to red cell mass parameters. The preflight Cr^{51} half-times of the Gemini VII astronauts were within our normal range; however, the postflight half-times were considerably longer. This suggests that a different population of red cells, with respect to age, absorbed the Cr^{51} following the flight. This infers that the mean age of the red cells had decreased during the flight interval. Because of the way the survivals were derived, the difference could not be a result of an altered production rate.

Table III shows the plasma volume changes of the Gemini astronauts. The preflight plasma volume of the Gemini IV pilot was 1074 ml greater than the predicted normal; however, his plasma volume continued to be proportionally greater than the estimated value postflight, a finding consistent with his superb physical condition. The preflight plasma volumes of the other flight crews were relatively close to their predicted normals.

Decreases in the plasma volumes, postflight, were noted in the astronauts who participated in Gemini missions IV and V, whereas the plasma volumes were increased when measured immediately after the Gemini VII flight. Plasma volumes determined several weeks after the recovery of the Gemini VII crew showed a rise above both the preflight and postflight values; however, these last samples were obtained within an hour of lunch and therefore cannot be directly compared to the fasting samples obtained previously.

Table IV shows the ratios of total body to peripheral venous hematocrit obtained during the Gemini V and VII series. These ratio changes suggest that the derived red cell mass changes, noted in Gemini IV, may have been overestimated if similar ratio changes can be extrapolated back to the IV mission. This initial overestimation was due to a decreasing hematocrit ratio resulting in an apparent decrease in the derived red cell mass. Postflight, the peripheral venous hematocrits, which were used to determine these ratios, decreased in three of the four astronauts. The venous hematocrits of the Gemini IV astronauts were also decreased and averaged 0.44 preflight and 0.42 postflight.

TABLE I. - RED CELL MASS CHANGES

	Predicted normal	Preflight	Postflight	Difference
Gemini IV				
CP	2180	2236[a]	1976[a]	-260
P	2332	3084[a]	2666[a]	-418
Gemini V				
CP	1953	1913	1530	-383
P	1904	2006	1565	-441
Gemini VII				
CP	2048	2077	1682 (2045)	-395 (-32)
P	2147	1969	1825 (2046)	-144 (+77)

[a]Derived from plasma volumes.
Values in parentheses indicate results 18 to 20 days postflight.
All values are expressed in milliliters.

TABLE II. - CALCULATED Cr^{51} RED CELL HALF-TIME IN DAYS

	Preflight	During flight	Postflight
Gemini V			
CP	-	18.0	-
P	-	16.6	-
Gemini VII			
CP	25.0	18.5	33.0
P	25.5	25.5	32.0

Normal 22 to 29 days.

TABLE III.- PLASMA VOLUME CHANGES

	Predicted normal	Preflight	Postflight	Difference
Gemini IV				
CP	2890	2962	2844	-118
P	2938	3885	3393	-492
Gemini V				
CP	2388	2354	2145	-209
P	2328	2300	2194	-106
Gemini VII				
CP	2502	2341	2760 (3232)	+419 (+891)
P	2624	2673	2774 (3260)	+101 (+587)

Values in parentheses indicate results 18 to 20 days postflight. All values are expressed in milliliters.

TABLE IV.- PERIPHERAL VENOUS HEMATOCRIT VALUES AND

TOTAL BODY/PERIPHERAL HEMATOCRIT RATIO

	Preflight		Postflight	
	Peripheral hematocrit	Ratio	Peripheral hematocrit	Ratio
Gemini V				
CP	.46	.98	.47	.89
P	.48	.98	.46	.91
Gemini VII				
CP	.46	1.02	.45	.84
P	.49	.86	.47	.85

Ratios calculated by dividing total body hematocrit $\left(\dfrac{\text{Red cell mass}}{\text{Red cell mass + plasma volume}} \right)$ by peripheral venous hematocrit.

DISCUSSION

From the derived red cell masses obtained after the Gemini IV
flight to the directly measured red cell masses obtained from the
Gemini V and VII missions, all pilots showed a red cell mass decrease
over their flight intervals. Quantitatively, the derived red cell
masses decreased 12 percent after the 4-day Gemini IV flight; however,
this value may be too high. Subsequently, a 20 percent red cell mass
decrease was found after the 8-day Gemini V flight, suggesting a linear
time dependent decrease. However, beyond the eighth day, the decrease
in red cell mass did not continue. One pilot of Gemini VII showed a
19 percent loss in red cell mass, whereas the other crewman's red cell
mass decreased only 7 percent. It should be noted, however, that the
latter pilot's red cell mass was 10 percent below the anticipated
normal. His was the only preflight red cell mass that was significantly
different from the calculated norm. In the three "typical" crewmembers
of Gemini V and VII, the decreases in red cell mass were accompanied by
shortened red cell half-times as measured by the Cr^{51} technique. The
red cell mass, of the one Gemini VII astronaut showing significant red
cell mass loss during flight, had returned to the preflight values within
3 weeks after his recovery. The other Gemini pilot did not lose a sig-
nificant portion of his red cell mass, but by 3 weeks postflight had
exceeded his preflight value by 77 ml, a figure of dubious significance.

Prior to the flight of Gemini VII, the percentages of reticulocytes
in the peripheral blood were determined on four occasions (T-10, 9, 4,
and 2 days). All reticulocyte percentages during this interval were
between 0.7 and 1.1 percent. For 2 days postflight, the reticulocyte
counts of either astronaut showed no change, but by the third day, the
reticulocyte percentage of the command pilot had risen to 1.4. The
reticulocyte percentage of the command pilot's blood subsequently rose
to 3.4 percent by the 18th and final day of observation. The pilot's
reticulocyte percentage 20 days after recovery was only 1.3 percent.
These later reticulocyte percentages correlate well with the observed
red cell mass losses and show a significant increase over the preflight
and the two early postflight values. The reticulocyte response corrobo-
rates the results obtained from the late red cell mass determinations
which showed the red cell masses returning toward normal. Hematolog-
ical studies performed on Gemini VII showed that the mean red cell
volume increased during the flight interval proportional to the red
cell mass loss. Although this change would tend to obscure the extent
of red cell mass reduction, it is added evidence that the total number
of circulating red cells was significantly reduced.

There are four possible mechanisms which could explain the decrease in the red cell mass seen in these studies. (1) Reduced red cell production with a normal red cell destruction rate; (2) normal production with an increased red cell destruction rate; (3) bleeding, either externally or into the interstitium; or (4) inadequate mixing of the radioactive cells used in the red cell mass determination. (This latter event would yield spurious low red cell mass values due to an effective "loss" of tagged red cells unavailable to the 15-minute mixing space of the vascular compartment.)

We have no clinical evidence to suggest that part of the intravascular red cells were sequestered and separated from the 15-minute distribution space of reinjected radioactive red cells. The evidence against this, however, is twofold: (1) surface counting immediately following the Gemini VII radioactive red cell injection, using a scintillation detector placed over the heart, showed an early equilibrium value which remained unchanged for a prolonged period; and (2) the red cell radioactivity per ml of red cells remained nearly constant between the 15-minute and the 24-hour samples, showing that good mixing had occurred within the first 15 minutes. Thus, any hypothesis based on inadequate mixing or reappearance of sequestered portions of the total red cell mass would seem unlikely. Bleeding internally or externally is neither plausible nor supported by the clinical findings. The fecal specimens obtained during the Gemini V flight were guaiac negative and insignificant amounts of Cr^{51} were found in them.

The demonstration of a shortened Cr^{51} red cell $T_{1/2}$ with an associated decrease in red cell mass offers substantiation for the theory of increased red cell destruction as the cause of these changes. No direct inflight measurements were made that would provide information about changes in the production rate of erythrocytes. By performing total red cell masses preflight and postflight, thereby correcting the Cr^{51} red cell half-times to total circulating red cells, we have eliminated a decreased production rate as the cause of the observed shortened half-times. Immediately following these flights, reticulocyte count percentages were approximately equal to those obtained preflight, supplying more inferential evidence against a decrease in red cell production during flight. Rigorous proof, however, that production does not decrease will have to await studies on future flights.

There is little information in the literature on red cell mass changes associated with bed rest and in only one study were red cell masses directly measured. For that bed rest study, the red cell mass

decreased 15 percent during the first 4 days of bed rest. However, multiple blood specimens were drawn prior to the determination, thus part of this decrease may be a result of experimental design rather than an effort of bed rest per se. Further work will have to be done before it is possible to state whether the red cell mass changes are caused by the inactivity of space flight or to other unknown factors.

The plasma volume changes following these flights were more variable than were the red cell mass changes. The Gemini VII mission showed conspicuous increases in plasma volume postrecovery; particularly the late determinations. The late determinations were done with the astronauts performing normal duties and in the postpradial state. It is possible, therefore, that this increase may be influenced by the time of day, activity, state and recent ingestion of liquid. During the Gemini VII mission, the pilots were not only in space for a longer period of time but spent many days out of their space suits, thereby reducing their thermal load. It is interesting that the plasma volume increases, noted during the Gemini VII mission, augmented the decreased red cell masses sufficiently to bring the blood volumes back to preflight values. Therefore, one can speculate that the plasma volume increase was of a compensatory nature, effective in reconstituting the blood volume. Decreases in plasma volume after Gemini IV and V would be expected if the plasma volume changes of space flight are similar to those of bed rest and water immersion. In one bed rest study, plasma volume was shown to decrease 10 percent after 4 days and 13 percent after 10 days, although other authors have reported greater changes. The decreases in plasma volume seen after Gemini IV and V were within the spectrum of change seen with similar periods of bed rest.

The plasma volume changes noted after these flights were not great enough to be a major cause of postflight orthostatic intolerance as demonstrated by passive tilts. Because the Gemini VII plasma volumes increased during the flight, resulting in essentially normal blood volumes, hypovolemia prior to tilt could not be instrumental for any orthostatic intolerance noted in these crewmen. Still unproven is the possibility that changes in capillary permeability allow effusion of plasma proteins from the vascular space into the interstitium at a rate rapid enough to affect cardiovascular function. Plasma volumes were not obtained immediately following tilt in these astronauts and no information is available to prove this.

During bed rest studies, the peripheral venous hematocrit increases. This is interpreted as evidence that the plasma volume decrease is greater than the concomitant loss in red cell mass. The hematocrits of four of the six flight crewmembers decreased postflight confirming the Cr^{51} red cell mass decreases found. This would indicate the red cell

mass changes are equal to or exceed the plasma volume changes. The dramatic changes of the ratio of total body to peripheral venous hematocrit found, preflight and postflight, in the crews of Gemini V and VII demonstrate a red cell mass cannot be calculated in this way, unless there is assurance that the ratio of total body to peripheral venous hematocrit remains constant.

For the Gemini IV mission, only plasma volume was directly measured. Using the venous hematocrit and the plasma volumes, derived blood volume and red cell mass were calculated. If a 10 percent change in the hematocrit ratio had occurred during the Gemini IV flight, as it did in the other two flights, the calculated red cell mass changes would have been 40 and 122 ml rather than the calculated values of 260 and 418 ml. Because a direct red cell mass was not ascertained, we have no information as to which value is most correct. This shows, again, the potential error of calculating red cell mass by the indirect method. Whether a similar change of hematocrit ratio occurs in subjects during bed rest is unknown, because in only one study were red cell masses directly measured. The uncertainty in the volume of red cell loss found in Gemini IV leaves unanswered the question of how soon and how rapidly the red cell loss occurs.

SUMMARY

The Gemini flights have given medical investigators a preliminary opportunity to measure the red cell mass and plasma volume changes associated with orbital flight.

During the Gemini flights, a consistent time related decrease in red cell mass has occurred. The cause of this decrease of red cell mass is not completely understood.

Plasma volume changes similar to those seen during bed rest were found after the Gemini IV and V flights. Similar changes were not found after Gemini VII for reasons as yet unknown. It would appear, therefore, that the orthostatic intolerance to passive tilt, seen in the pilots after their return, cannot be explained by changes of plasma volume.

APPENDIX

ml   – milliliter   Bkg – background radioactivity

Pl   – plasma   Std – standard

Wh Bl – whole blood   Spec – specimen

RBC   – red blood cells   Syr – syringe

Hct   – hematocrit expressed as a decimal

NCPM – net counts per minute

      (gross counts per minute of sample tube – gross counts per minute of empty tube)

NOTE: When the subject has had a previous radioisotope study, a background blood is drawn. Then the subject's own blood or plasma counts are subtracted instead of the counts of an empty tube.

Plasma volume:

$$Pl\ vol = \frac{(NCPM/ml\ Std = Dilution\ Factor) + NCPM\ Std\ Syr - NCPM\ Spec\ Syr}{NCPM/ml\ 15\ minute\ Pl\ Spec}$$

Red cell mass:

$$RCM = \frac{A\ x\ Amt\ Inj}{B}\ x\ Spec\ Hct$$

A = NCPM/ml Std Wh Bl – NCPM/ml Std Pl x (1–Std Hct)

B = NCPM/ml Spec Wh Bl – NCPM/ml Spec Pl x (1–Spec Hct)

Percent of remaining Cr^{51} tagged red cells on day X

$$\% = \frac{RCM\ (on\ day\ X)\ x\ C}{RCM\ (on\ day\ O)\ x\ D}$$

C = NCPM/ml RBC (on day X)

$$= \frac{\text{NCPM/ml Wh Bl (on day X)} - \text{NCPM/ml Pl (on day X)} \times (1-\text{Hct (on day X)})}{\text{Hct (on day X)}}$$

D = NCPM/ml RBC (on day 0)

$$= \frac{\text{NCPM/ml Wh Bl (on day 0)} - \text{NCPM/ml Pl (on day 0)} \times (1-\text{Hct (on day 0)})}{\text{Hct (on day 0)}}$$

Cr^{51} Red blood cell half-time in days

$$T_{1/2} = \frac{.693t}{\ln\left(N_0/N_X\right)}$$

t   = time elapsed from day 0 to day X

N_0 = 100%

N_X = percent of Cr^{51} tagged red cells remaining on day X

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GEMINI M-5 EXPERIMENT

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Observations of readily recoverable weight losses and orthostatic hypotension following orbital space flights of relatively short duration led to a series of ground-based studies to simulate some of the conditions of space flight. Also, an attempt was made to define the physiological parameters which would be affected by the condition of weightlessness. These studies centered about bed rest and immersion as means of simulating the effect of weightlessness on the cardiovascular system and, at least in immersion studies, the effect on the musculo-skeletal system.

The observations led to the inclusion of inflight urine collections and the determination of total urine production as part of the inflight medical experiments. The Experiment M-5 was flown on Gemini VII (14 days of flight) and will be flown on at least two 3-day flights. In addition to other determinations, the experimental protocol calls for the determination of preflight and postflight plasma electrolytes and ADH, preflight, inflight, and postflight urinary electrolyte determinations, and preflight and postflight urinary aldosterone.

At the present time, the results of the inflight part of the Gemini VII experiment are not complete. The data that are available provide us with water consumption and a rough estimate of the urine production as measured by an inline flow meter. The calculation of urine production by isotope dilution is still being made.

Prior to the Gemini VII flight, preflight and postflight plasma samples were obtained from crews of Gemini IV, V, and VI and the electrolytes were determined.

Sodium and potassium were determined by flame photometry. Chloride was determined by the Cotlove coulometric method and calcium was determined by the Ferro-Ham procedure.

All results were within the normal ranges and there were no discernable trends within the limited number of the available samples. Figures 1 and 2 present the analytical results of preflight and postflight plasma samples obtained from the crew of Gemini VII. There are no gross deviations in the electrolytes.

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GEMINI VII PLASMA
ASTRONAUT F BORMAN

	PRE-FLIGHT		POST-FLIGHT			
	11/25	12/2	12/18 (1130)	12/18 (1820)	12/19	12/21
Na (meq/L)	147	146	138	140	144	143
K (meq/L)	4.7	5.4	4.1	4.7	4.7	4.9
Cl (meq/L)	103	103	100	102	103	106
PO$_4$-P (mg%)	3.2	3.7	4.0	4.2	3.1	3.6
Ca (mg%)	9.0	9.2	8.6	9.2	9.0	9.2
UREA N (mg%)	19	16	16	20	25	18
URIC ACID (mg%)	6.8	6.6	4.6	6.0	5.9	6.0
TOTAL PROTEIN (gm%)	7.3	7.4	6.8	7.6	7.0	7.1
ALBUMIN (gm%)	4.7	4.9	4.2	QNS	4.5	4.6
17-OH CORTICOSTEROIDS (µg/100 ml)	18.8		28.3	16.0		
HYDROXY PROLINE µm/ml:						
FREE	0.008	0.007	0.010	0.011		
BOUND	0.131	0.146	0.151	0.185		
TOTAL	0.139	0.153	0.161	0.196		

Figure 1

GEMINI VII PLASMA
ASTRONAUT J LOVELL

	PRE-FLIGHT		POST-FLIGHT			
	11/25	12/2	12/18 (1230)	12/18 (1800)	12/19	12/21
Na (meq/L)	149	146	139	144	143	144
K (meq/L)	4.9	5.1	4.1	5.0	5.5	5.0
Cl (meq/L)	104	103	97	101	100	104
PO$_4$-P (mg%)	3.1	3.3	3.9	3.9	3.4	3.4
Ca (mg%)	9.6	9.6	9.2	9.4	10.0	9.6
UREA N (mg%)	23	22	21	28	27	24
URIC ACID (mg%)	6.1	5.8	3.8	5.3	5.0	5.0
TOTAL PROTEIN (gm%)	7.8	7.8	7.2	7.9	8.1	7.2
ALBUMIN (gm%)	4.8	4.7	4.3			
17-OH CORTICOSTEROIDS (µg/100ml)	13.3		26.2	8.9		
HYDROXY PROLINE µm/ml:						
FREE	0.017	0.010	0.010	0.005		
BOUND	0.161	0.167	0.182	0.187		
TOTAL	0.178	0.177	0.192	0.192		

Figure 2

Sodium and potassium are slightly lower than preflight but are still normal and do not form a part of any trend. We can conclude that up to 14 days of orbital space flight does not result in any gross aberrations of plasma electrolytes.

Figures 3 and 4 present preflight and postflight analyses of urine from the Gemini VII crew. The values are the sum of results of individual samples from approximately 24-hour periods. The first day postflight was taken from the first voiding following recovery.

For 24-hour period postflight, there was marked water retention. The output for each case was approximately 1 liter less than the preflight 24-hour volume. In addition, there was marked retention of chloride, sodium, and potassium. Potassium retention is far more marked in the case of the pilot than the command pilot.

Concommitant with the analyses presented in these figures, ADH and urinary aldosterone were assayed by the Baylor University School of Medicine's endocrinology laboratory. The only sample containing measureable quantities of ADH was the pilot's urine immediately following recovery. Urinary aldosterone was increased in the postflight samples (see table I).

TABLE I.- ALDOSTERONE

Command Pilot	Pilot
Preflight = 28 γ/24 hour	Preflight = 21 γ/24 hour
23 γ/24 hour	35 γ/24 hour
	31 γ/24 hour
Postflight = 75 γ/24 hour	Postflight = 47 γ/24 hour
28 γ/24 hour	60 γ/24 hour

Postflight water retention is consistent with the concept that the weight loss during flight and its rapid recovery is caused by water loss during flight. There is not sufficient data to determine whether the loss resulted from diuresis during flight or through sweating and insensible losses. We hope to have this answered through analysis of

GEMINI VII URINE
ASTRONAUT J LOVELL

	PRE-FLIGHT		POST-FLIGHT	
	11/23	11/30	12/18	12/19
CI (meq)	177	139	40	45
Ca (mg)	182	126	115	207
URIC ACID (g)	0.91	1.14	0.45	0.92
TOTAL VOLUME (ml)	1912	1737	735	1405
Na (meq)	162	145	35	58
POTASSIUM (meq)	76	93.0	44	58
PO_4-P (gm)	1.12	1.27	0.80	1.07
17-HYDROXYCORTICOSTEROIDS	8.0	9.07	7.83	8.33
TOTAL N (gm)	19.94	21.6	12.81	22.8
UREA N (gm)	17.19	17.06	11.75	21.51
HYDROXYPROLINE (mg)	39.39	43.1	31.8	37.4
CREATININE (gm)	2.27	2.25	1.75	2.16

Figure 3

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GT-VII URINE
ASTRONAUT FRANK BORMAN

	PRE-FLIGHT		POST-FLIGHT	
	11/23	12/1	12/18	12/21
Cl (meq)	144	148	61	145
Ca (mg)	254	266	310	268
URIC ACID (g)	0.96	0.95	1.20	1.07
TOTAL VOLUME (ml)	2920	3235	2160	3690
Na (meq)	141	146	64	133
POTASSIUM (meq)	93.0	79	73	106
PO$_4$ -P (gm)	1.13	1.16	1.72	1.12
17-HYRDOXYCORTICOSTEROIDS	6.9	8.76	13.69	9.28
TOTAL N (gm)	19.2	22.6	30.9	20.5
UREA N (gm)	18.1	18.5	26.6	18.7
HYDROXYPROLINE (mg)	48.74	37.0	65.4	39.9
CREATININE (gm)	2.11	2.11	2.86	1.80

Figure 4

urine output by the Gemini VII crew and crews of subsequent shorter flights. However, the water, sodium, and potassium retention equate with the observation of Vogt and his coworkers who observed diuresis along with sodium and potassium excretion occurring early during recumbency studies.

The complexity of the mechanisms for electrolyte regulation and the paucity of data make it difficult to provide more than a simple hypothesis to explain the observations we have made.

1. After relatively short periods of earth orbit, the astronaut exhibits a loss of weight.

2. This loss, as observed on several flights to date, does not appear to be progressive with the duration of the mission.

3. It is rapidly recovered postflight.

4. The recovery, as observed on the Gemini VII crew, is accompanied by water and salt retention.

5. It is also accompanied by an increase in urinary aldosterone.

These data are consistent with the hypothesis that atrial and thoracic stretch receptors are of physiological importance in the change from 1g to zero g and back again. The change from zero g to 1g would result in an apparent decrease in thoracic and atrial blood volume triggering the increased output of ADH and aldosterone resulting in water and salt retention. The reverse, going from 1g to zero g is probable and should resemble the early diuresis and salt loss found in the recumbency studies. At least, a partial resolution of the mechanism should be found in the analysis of urine volumes and electrolyte output during the Gemini VII flight, and during the subsequent short-term flights.

SUMMARY

The data, as of this date, are far from complete. Virtually no change in blood chemistries occur preflight and postflight. The data are consistent with results of recumbency experiments and indicate that the Auer-Henry reflex may be involved.

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THE EFFECTS OF RECUMBENCY AND SPACE FLIGHT ON BONE DENSITY

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This is a report of the method by which bone mass changes were studied in healthy young men who were used as test subjects for a series of bed rest studies conducted at the Texas Woman's University, and the manner these bone changes were used for comparison with the bone mass changes which were found from preflight and postflight radiographs of the Gemini IV, V, and VII astronauts.

TEXAS WOMAN'S UNIVERSITY BED REST UNITS

For approximately 3 years healthy men between 20 and 42 years of age were used for bed rest studies conducted at the Texas Woman's University Research Institute. Seven 14-day and two 30-day bed rest periods were followed and a 42-day bed rest investigation based on a moderately low calcium intake is planned for the near future.

The daily levels of calcium for the 14-day bed rest units were 300 milligrams, 500 milligrams, 700 milligrams, 800 milligrams, 1.0 gram, 1.5 grams, and 2.0 grams, respectively. During the two 30-day bed rest periods, 1.0 gram and 2.0 grams of calcium were fed.

General Plan of a Bed Rest Unit

Before each bed rest period, the subjects are equilibrated with respect to level of bone mass in the central section of the os calcis on a diet of relatively high calcium content, which has been standard for all bed rest units. Usually it takes from 2 to 3 weeks to bring the men to a constant bone density level. After a bed rest has been completed, the subjects are reconditioned at the same calcium level as was followed during the preliminary equilibration phase.

During the bed rest period, the subjects use only one pillow and they remain recumbent throughout this phase of the study. They are bathed in bed, and have their teeth brushed and all hygienic needs cared for by trained male orderlies. The subjects watch their respective hospital television sets, and read by means of glasses equipped with prismatic lenses. The lenses permit a person to read while lying flat on his back by looking up through the glasses at a book lying on his lower chest.

The subjects are spoon fed by the dietitians who do not force the subjects to eat the carefully planned food. The dietitians encourage, but without undue stress, the subjects to eat the food.

Tests Used on Bed Rest Units

The major tests of the bed rest subjects were: measurements of the changes in bone mass by radiographic bone densitometry; chemical tests for calcium and phosphorus in food and excreta; and, urinary tests for nitrogen, creatine, creatinine, 17-ketosteroids, and 17-hydroxy-corticosteroids. Cardiovascular tests were made on some of the bed rest units and the tests included tilts and blood volume assessments. Blood volume assessment used isotopic iodine and the cardiovascular tests were conducted under the direction of Fred B. Vogt, M.D.

In determining the status of calcium and phosphorus balance, urinary analyses, alone, are not used but fecal determinations are also made. Although there are variations among individuals and within the same individual from one time to another, it has been found in these immobilization bed rest studies that more than three-fourths of the excreted calcium is in the feces. But, between 60 and 75 percent of the excreted inorganic phosphorus is found in the urine.

DIETARY VARIABLES IN THE STUDY

Dietary calcium has been the main variable throughout the study at this point but the intake of phosphorus is regulated to maintain a calcium to phosphorus ratio which is within acceptable textbook limits. Other major nutrients were standardized in the various bed rest units on the basis of optimum levels. Carbohydrate intake was regulated to keep energy consumption compatible with the needs of the subject. Because the astronaut varies his intake of nutrients other than calcium and phosphorus when he does not consume all of the food provided in the spacecraft, it was suggested that other nutrients should serve as variables for our bed rest studies.

Method of Evaluating Bone Mass

Bone mass (in terms of calibration wedge equivalency in grams) is evaluated from carefully exposed radiographs by means of a densitometer equipment assembly. This equipment is a special analog computer consisting of subassemblies which are designed to operate together as an integrated system. This is the sixth in a series of densitometric assemblies developed by Dr. Mack and her colleagues. The first equipment of the series was reported in 1939 and the theoretical aspects of the method used were described by Mack, Brown, and Trapp. The historical development of the method and technique to 1950 was reported by Dr. Mack; Mack, Vose, and Nelson, as well as Mack, have covered this technique through the following decade and have described the instrumentation used in the current investigation.

The equipment consists of four basic units, which are:

1. A modified Knorr-Albers scanning unit.

2. A Speedomax Model G transmitting recorder, which produces the film density curve and contains within the same panel a series of potentiometers used for the purpose of correcting the nonlinear density curve.

3. A Speedomax Model G recorder for displaying the curve.

4. An Instron Integrator geared to the output of the second recorder.

Figure 1 shows a part of the densitometer assembly.

The sequence of operations needed to achieve linearization of a density curve and to integrate the area under the curve of a bone on the same radiograph is:

1. The wedge X-ray image first is scanned for the purpose of providing the density curve of that film on the first recorder.

2. Then the technologist measures the displacement from a standard trace which conforms to the straight line slope of the wedge at 20 points along the chart baseline, and sets the respective potentiometers in the panel associated with each of the points. This is facilitated by the use of a scale, which shows the deviation of the scan from linearity at each point, thus indicating the correct potentiometer setting required to obtain the needed resistance for a section of a major slidewire within the instrument geared to each of the 20 points on the curve mentioned above. This is facilitated by the use of a scale,
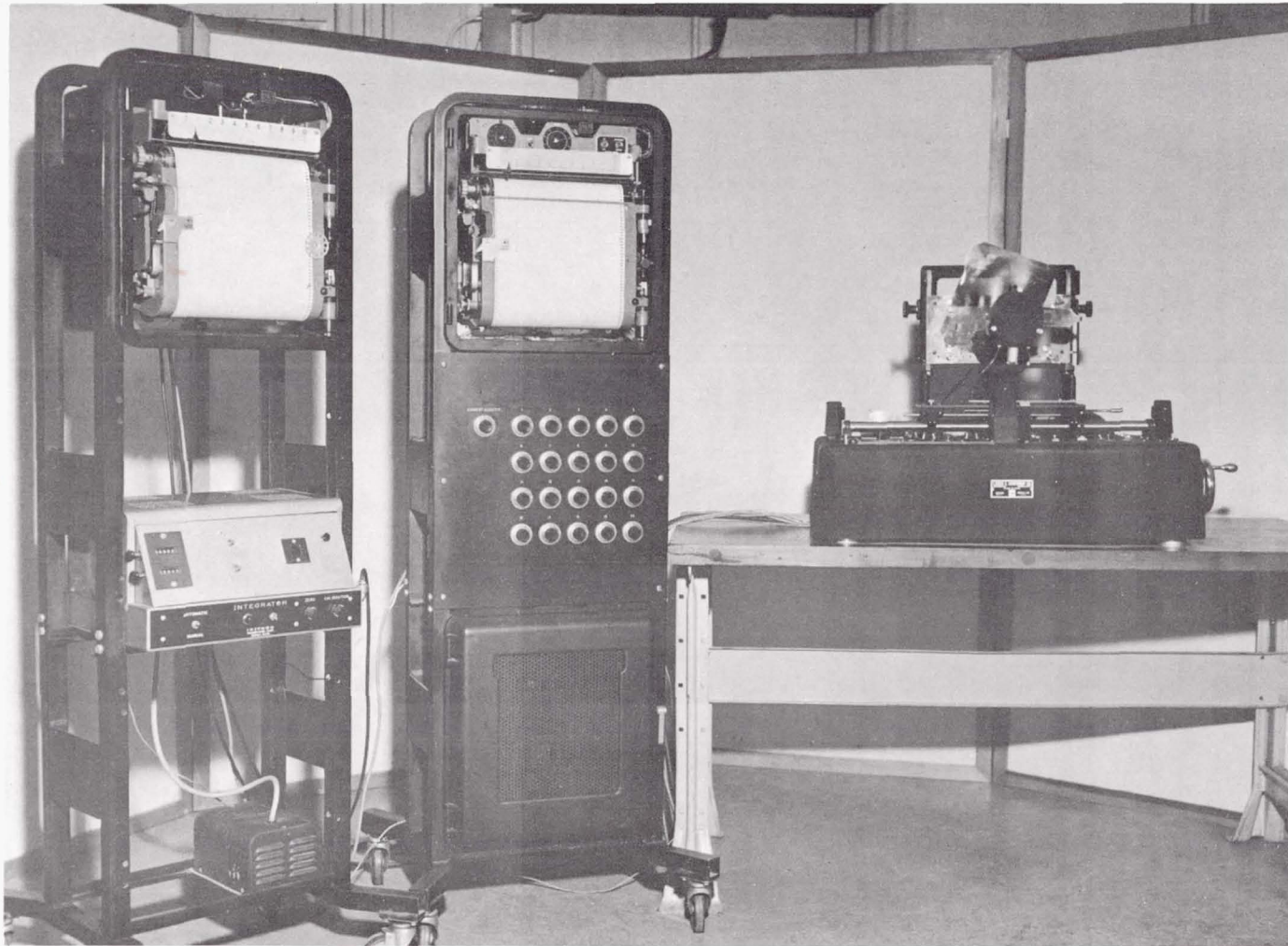
Figure 1. - Densitometer.

which shows the deviation of the scan from linearity at each point, thus indicating the correct potentiometer setting required to obtain the needed resistance for a section of a major slidewire within the instrument geared to each of the 20 points on the curve.

3. To check the linearity of the corrected curve the wedge image is traced again on a chart on the second recorder.

4. When the wedge tracing displayed on the second panel is corrected to a straight line, the desired section of the bone then is scanned with its trace that is also shown on the second recorder. The scan is evaluated simultaneously by means of a readout count obtained from an Instron Integrator situated in the lower part of the second recorder panel of the instrumentation.

Standardization of X-Ray Units and Radiographs

When more than one X-ray unit is used in taking serial radiographs that are to be used for comparative purposes, as are the astronauts who must be filmed before their orbital flight at Cape Kennedy and on the aircraft carrier immediately after recovery from an orbital flight, and at the Manned Spacecraft Center after their flight, the X-ray units and procedures must be standardized.

The three methods of standardization are: an aluminum alloy calibration wedge is exposed on each film adjacent to the bone; a Victoreen roentgen meter is used immediately before making a radiograph to determine the calibrated kilovoltage which would produce identical X-ray beam qualities with all X-ray units used; and, by exposing at each testing period a phantom composed of a simulated os calcis having calcium hydroxyapatite distributed through an organic matrix. For the os calcis, for example, milliamperes, kilovolts, and time are set to give an exposure level of 167 ± 2 milliroentgens.

Radiographs Made of TWU Bed Rest Subjects and Astronauts

In the Texas Woman's University bed rest studies, frequent radiographs are made at various anatomical sites. These sites include the left os calcis in lateral projection, the left hand in posterior-anterior aspect, and the lateral view of the knee. The lumbar spine and the neck of the femur are radiographed less frequently. Because only 167 milliroentgens are required to X-ray the os calcis according to our technique and a lesser quantity is needed for the hand, X-rays are taken daily during a 14-day bed rest of these two sites. Less frequent radiographs are made during the initial equalibration and the final reconditioning periods.

Only the left foot and hand of the astronauts are radiographed. Various scans with the densitometer, each representing a section of bone the width of the scanning beam (1.3 mm) are made on these two radiographs. Figure 2 is a positive of a radiograph showing a scan made across a central portion of the os calcis between two distinct landmarks as well as another scan across the talus. We call this the "conventional" scan. Tracing across this path gives the bone mass, in terms of calibration wedge X-ray absorbency in grams of this section of bone.

Figure 3 is the positive of an os calcis, which illustrates the positions of a series of multiple scans parallel with the conventional scan. Each scan is 1.0 mm from the center of one scan to the center of the next scan. The sections of the os calcis, which theoretically are sliced off by these scans, cover about 60 percent of the total os calcis.

Figure 4 is the positive of a hand radiograph. Phalanges 5-2 and 4-2 are evaluated for X-ray absorbency of bone (in terms of calibration wedge equivalency) for this part of the anatomy. The parallel lines shown on the two phalanges illustrate the positions of the scans made by the densitometer beam on phalanx 5-2 and again on 4-2. As in the case of the multiple traces on the os calcis, the center of each scan is 1.0 mm from the center of the next scan, with the edges of the successive scans slightly overlapping. The sums of the integrator counts for the series of scans on each phalanx are used to calculate bone mass changes from the date of one radiograph to that of another.

Loss of Skeletal Mass in the Bed Rest Studies

The losses of bone mass (in terms of calibration wedge equivalency) for different periods of bed rest time when the men have received different daily levels of dietary calcium has served as a basis of comparison of losses from the same anatomic sites by the astronauts during orbital flight. Because daily X-rays are made daily during bed rest the changes in bone mass can be calculated for any number of days up to the length of time of the bed rest. Table I gives the average losses which were found during 4 days, 8 days, and 14 days, of men at bed rest on the designated levels of dietary calcium in the central os calcis section during the TWU bed rest units. Also, the losses for the two 30-day units, which have been completed, are included.

The changes in bone mass given in this report in terms of X-ray absorbency or of calibration wedge equivalency does not denote losses of calcium alone but of the chief mineral complex of bone, calcium hydroxyapatite $\left[3Ca_3(PO_4)_2 \cdot Ca(OH)_2\right]$, and water-organic components of

TABLE I

CHANGE IN BONE DENSITY IN THE CENTRAL OS CALCIS OF

BED REST UNITS FOR SPECIFIED NUMBER

OF DAYS

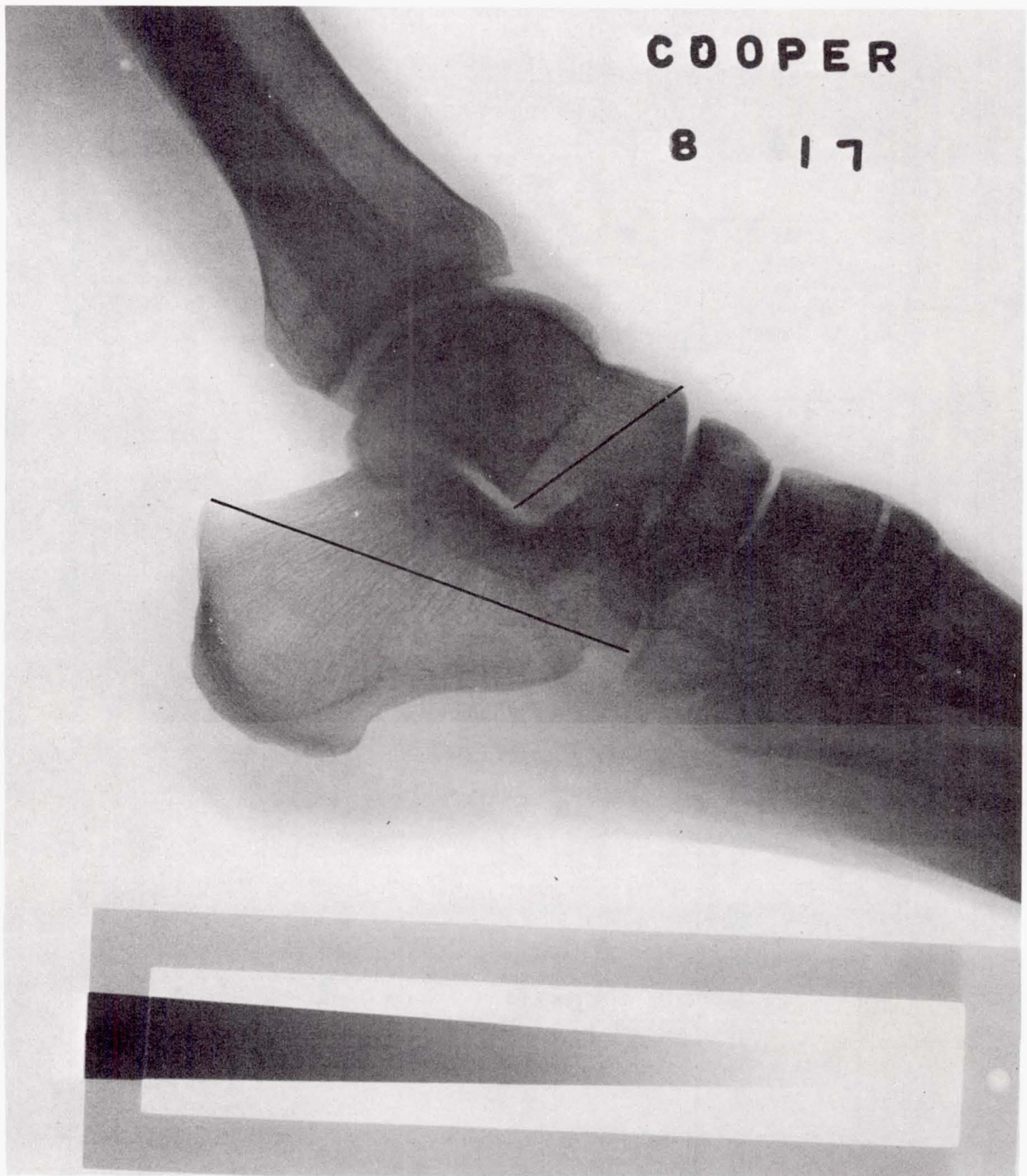| Level of Dietary Calcium Provided (milligrams)	Average Amount of Calcium Consumed (milligrams)	Days on Bed Rest Study	Average Change in Bone Mass on Designated Days
14-Day Bed Rest Units			
300 (4 subjects)	302	4 8 14	-6.25 -7.42 -12.35
500 (4 subjects)	432	4 8 14	-7.27 -7.14 -11.65
700 (4 subjects)	689	4 8 14	-3.47 -4.30 -7.67
1,000 (5 subjects)	987	4 8 14	-3.62 -2.66 -4.76
1,500 (4 subjects)	1,446	4 8 14	-2.57 -3.15 -5.96
2,000 (4 subjects)	2,012	4 8 14	-3.35 -3.79 -4.96
30-Day Bed Rest Units			
1,000 (5 subjects)	1,017	4 8 14 30	-2.41 -3.75 -5.28 -6.78
2,000 (5 subjects)	1,948	4 8 14 30	-2.21 -2.36 -3.89 -6.12

Figure 2. - Os calcis.
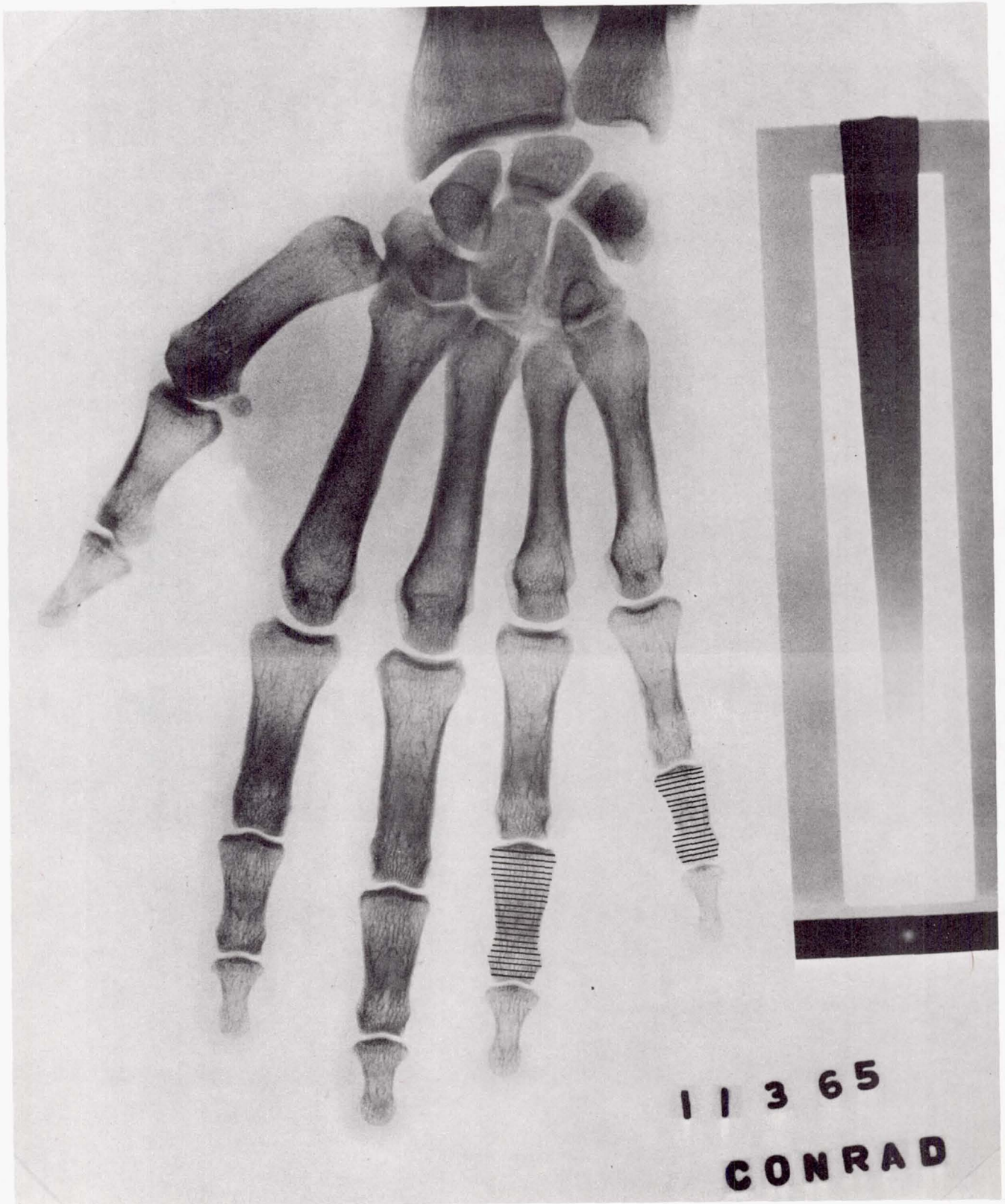
Figure 3. - Multiple scan os calcis.

Figure 4. - Hand X-ray.

the bone itself and of over- and under-lying soft tissue. In the major anatomical sites chosen for measurements from radiographs, the extra bone protein has only a slight effect upon the results because conditions of exposure are chosen so as to minimize the effect of organic materials and to maximize that of the mineral components.

Loss of Skeletal Mass of Gemini Astronauts in Comparison with Bed Rest Subjects

Use was made of this background bed rest information for comparing this with findings from Gemini IV, Gemini V, and Gemini VII orbital flights. For example, some of the Gemini astronauts have not eaten all of the food provided for them. Certain bed rest subjects have been found to have consumed calcium at approximately the same level. The losses in bone density of the central section of the os calcis of the astronauts and of the bed rest subjects who matched them in calcium consumption for the same length of time are shown in table II for Gemini IV and Gemini V.

Figure 5 includes a graph of the values for the "conventional" section of the os calcis for the command pilot and pilot of Gemini IV. Figure 6 illustrates the changes in bone mass of the two hand phalanges throughout the study of Gemini V.

The os calcis losses in the two astronauts of Gemini IV, as shown in table II, were 7.80 and 10.27 percent, respectively. The losses in the hand phalanges, in terms of calibration wedge equivalency, for the two men in the Gemini V mission were comparatively high. For both missions hand phalanx losses, particularly in Gemini V, greatly exceeded those in bed rest subjects which sustained extremely low losses in this anatomical site.

It should be noted that the astronauts of Gemini IV consumed only a mean of 679 and 739 milligrams, for the command pilot and the pilot, respectively, which did not represent the full diet provided for them. The corresponding levels of calcium consumption means for the Gemini V astronauts were 373 and 313 milligrams per day. This constituted between one-third and one-fourth of the calcium provided for them. In addition, they also were consuming about these same low levels of energy and of other major nutrients by eating such a low proportion of their total food.

The results of the study of the astronauts of Gemini VII will be given at the conferences on February 23, 24, and 25, 1966. Briefly, it should be noted that Gemini VII was the longest mission made in a manned spacecraft, and the losses in bone mass were less than the two

TABLE II

CHANGE IN BONE DENSITY IN THE CENTRAL OS CALCIS AND IN THE HAND PHALANX 5-2 IN ASTRONAUTS OF GEMINI IV AND GEMINI V AND IN BED REST SUBJECTS ON SIMILAR DIETARY CALCIUM LEVELS FOR THE SAME PERIOD OF TIME (FOUR DAYS)

PART A. GEMINI IV

Subjects	Level of Daily Calcium Intake	Change in Central Os Calcis Bone Density (per cent)
GEMINI IV		
Command Pilot	. . 679 . . .	. -7.80
Pilot . . .	. . 739 . . .	. -10.27
TWU BED REST		
SUBJECTS		
Subject 1 . .	. . 675 . . .	. -2.67
Subject 2 . .	. . 659 . . .	. -4.25
Subject 3 . .	. . 636 . . .	. -3.39
Subject 4 . .	. . 636 . . .	. -3.59

Subjects	Level of Daily Calcium Intake	Change in Hand Phalanx 5-2 in Bone Density (per cent)
GEMINI IV		
Command Pilot	. . 679 . . .	. -11.85
Pilot . . .	. . 739 . . .	. -6.24
TWU BED REST		
SUBJECTS		
Subject 1 . .	. . 675 . . .	. -1.61
Subject 2 . .	. . 659 . . .	. -1.80
Subject 3 . .	. . 636 . . .	. -2.28
Subject 4 . .	. . 636 . . .	. +1.61

TABLE II, CONCLUDED

CHANGE IN BONE DENSITY IN THE CENTRAL OS CALCIS AND IN THE

HAND PHALANX 5-2 IN ASTRONAUTS OF GEMINI IV AND GEMINI V

AND IN BED REST SUBJECTS ON SIMILAR DIETARY CALCIUM

LEVELS FOR THE SAME PERIOD OF TIME (FOUR DAYS)

PART B. GEMINI V

Subjects	Level of Daily Calcium Intake	Change in Central Os Calcis Bone Density (per cent)
GEMINI V		
Command Pilot. . .	373	-15.10
Pilot	333	-8.90
TWU BED REST SUBJECTS		
Subject 1 . . .	307	-8.65
Subject 2 . . .	292	-5.06
Subject 3 . . .	303	-7.89
Subject 4 . .	308	-8.06

Subjects	Level of Daily Calcium Intake	Change in Hand Phalanx 5-2 in Bone Density (per cent)
GEMINI V		
Command Pilot. . .	373	-23.20
Pilot	333	-16.97
TWU BED REST SUBJECTS		
Subject 1 . . .	307	-1.52
Subject 2 . . .	292	+0.08
Subject 3 . . .	303	-1.65
Subject 4 . .	308	-1.67
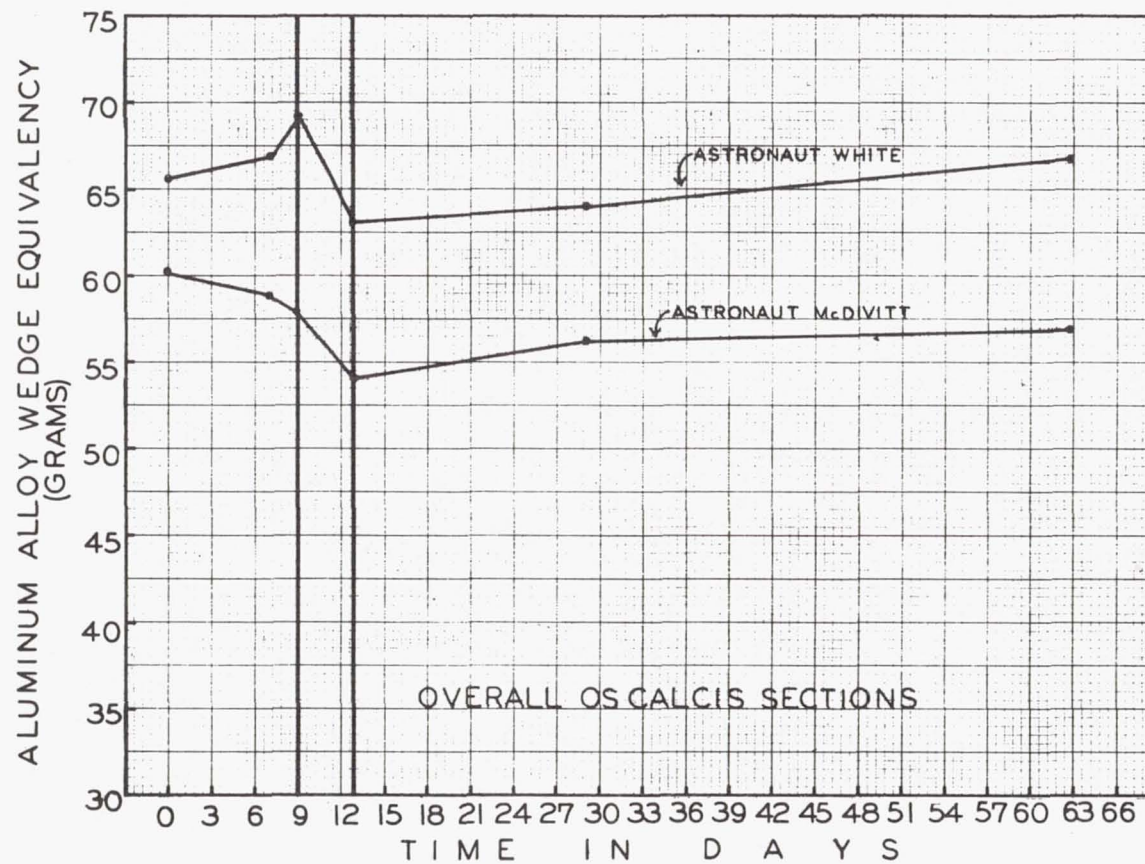
Figure 5. - Overall changes in bone in terms of mean aluminum alloy wedge equivalency of the entire series of parallel segments.
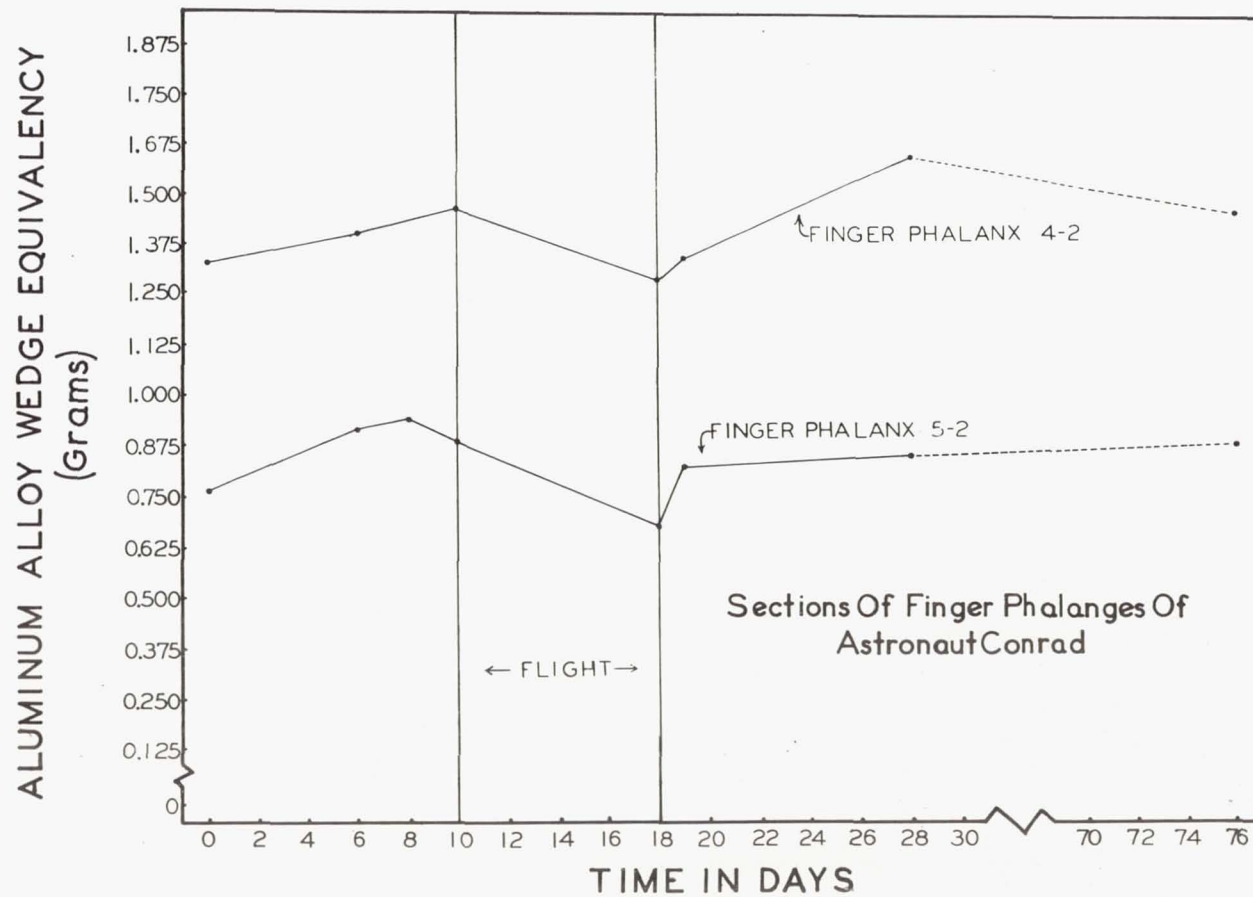
Figure 6. - Changes in the aluminum alloy wedge mass equivalency of hand phalanges 4-2 and 5-2 of Gemini V pilot.

previous flights of 4 and 8 days. The change in the "conventional" section of the os calcis was 2.91 percent for the command pilot and 2.84 percent for the pilot. The losses from the hand phalanges tended to be lower than for the men on the Gemini IV and Gemini V missions, particularly Gemini V, but were greater than the losses of the bed rest study subjects for this anatomical position.

We attribute the vast improvement in the retention of bone mass by the Gemini VII astronauts, at least in part, to the fact that they consumed a substantial portion of their food and they had routine isometric and isotonic exercise.

It should be stated that the bone losses shown in these orbital flight studies by no means represent any level of skeletal pathology. Within the studies conducted thus far, the bone mass returns to a pre-flight level within a relatively short period of time postflight.

GEMINI BONE DENSITOMETRY STUDY

CHANGE IN OS CALCIS DENSITY
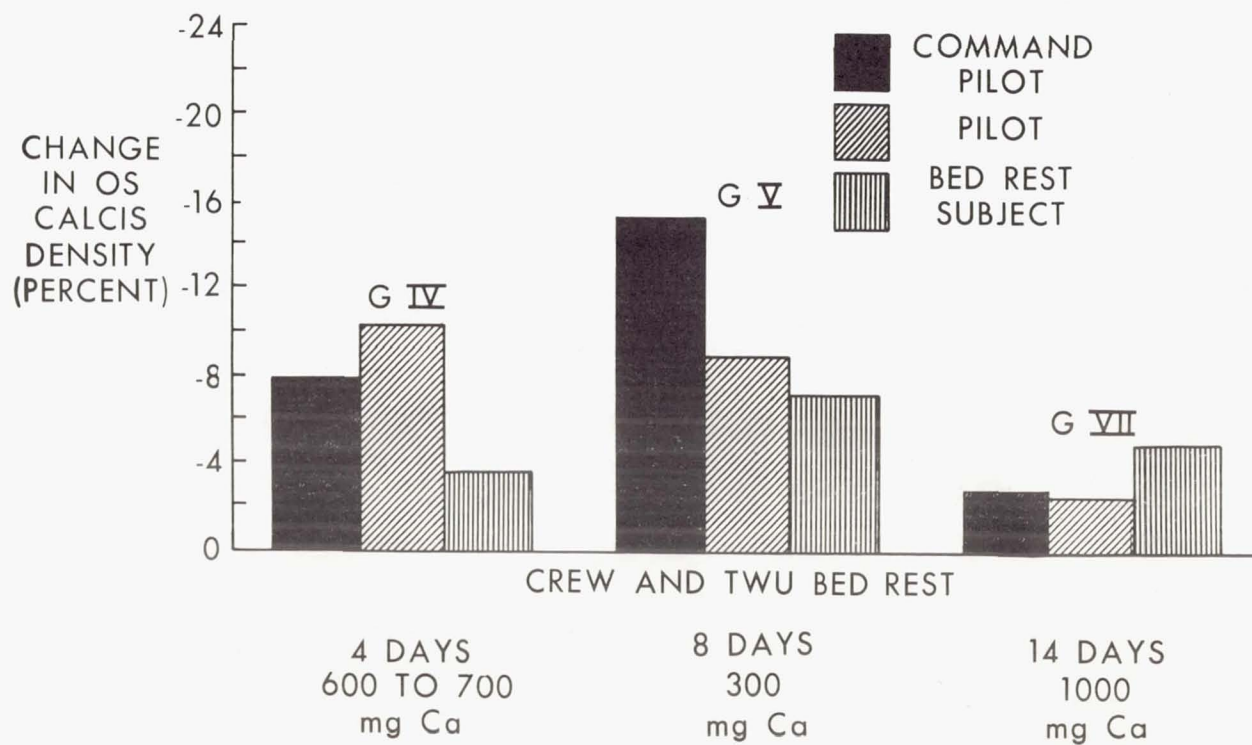
Figure 7

GEMINI BONE DENSITOMETRY STUDY
CHANGE IN DENSITY OF HAND PHALANX 5-2
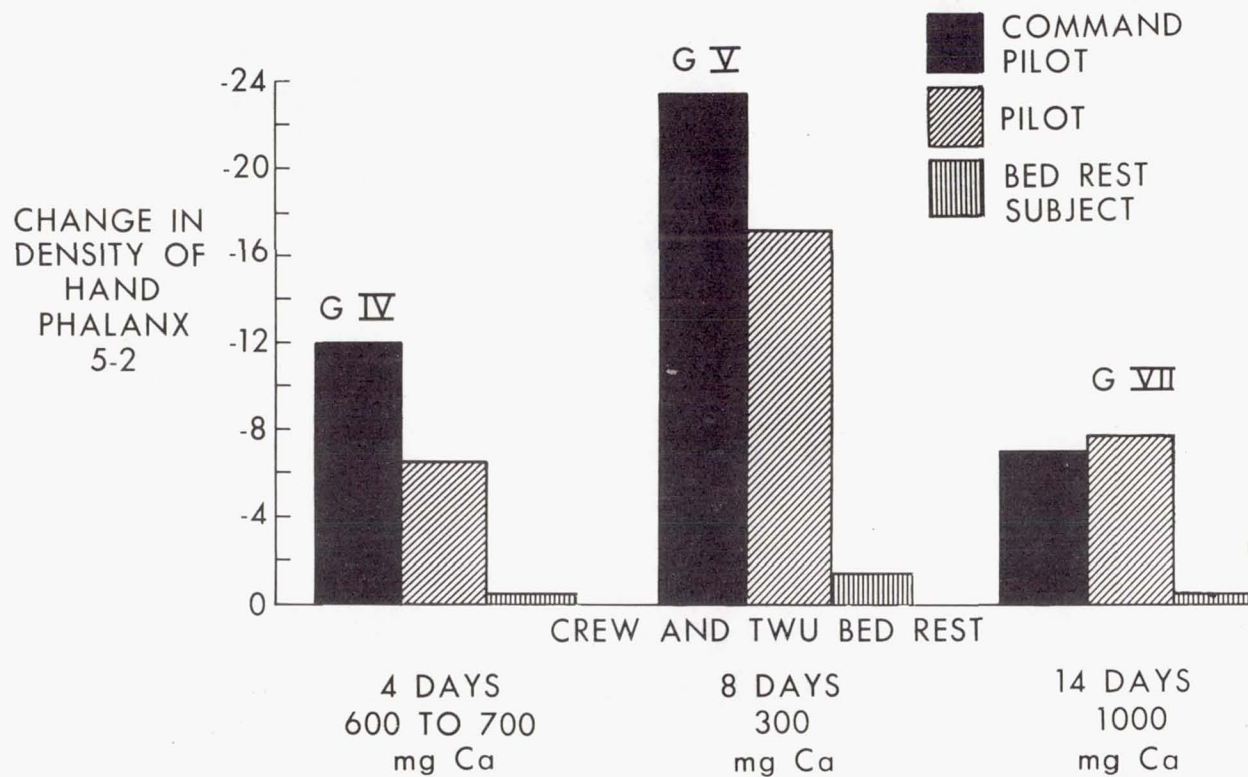
Figure 8

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1. Mack, Pauline Beery; O'Brien, Anne T.; Smith, Janice M.; and Bauman, Arthur W.: A Method of Estimating a Degree of Mineralization of Bones from Tracking Roentgenograms. Science, vol. 89, p. 467 (1939).

2. Mack, Pauline Beery; Brown, Walter N.; and Trapp, Hughes Daniel: The Quantitative Evaluation of Bone Density. Amer. J. of Roentgenology and Radium Therapy, vol. 61, p. 808 (1949).

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ELECTROENCEPHALOGRAM DURING ORBITAL FLIGHT:

EVALUATION OF DEPTH OF SLEEP

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The M-8 experiment conducted on the Gemini VII flight was our first attempt to record the electroencephalogram (EEG) of a pilot during orbital flight. The immediate and practical goal of this experiment is to obtain an objective measurement of the pilot's sleep pattern. The measurement was to discover any deviation from the normal sleep pattern of an astronaut and to try to assist in pinpointing any factors which may interfere with sleep in an orbiting spacecraft. Several astronauts reported that it has been difficult to sleep during flights. In addition to this practical goal, the experiment is also intended to determine the effects, if any, of weightlessness on the electrical activity of the brain.

The analysis of the data from the Gemini VII flight is not complete and definitive conclusions cannot be made at this time. The present report gives our preliminary evaluation of the data by visual analysis of the recordings. Computer analysis of the data is in progress by Dr. Ross Adey at University of California at Los Angeles and by Dr. Neil Burch at the Baylor University College of Medicine.

PROCEDURE USED ON GEMINI VII FLIGHT

Locations of Electrode Sites

Prior to the day of the flight, the helmet liner used by command pilot Borman was perforated at four electrode sites. The measurements for locating the electrode sites are:

Midline center site - 7.8 in. from the external auditory meatus in the coroneal plane and 7.9 in. anterior to the inion in the sagittal plane.

Midline occipital site - 1.6 in. superior to the inion in the midsagittal plane.

Left central site - 3.1 in. to the left of the midline central site
in the coronal plane.

Left occipital site - 1.4 in. to the left of the midline occipital
site.

At about 8:00 a.m., December 4, 1965, at the MSO building of
Kennedy Space Center, the helmet liner was fitted on the command pilot's
head and the perforations in the liner were used to mark the electrode
sites. This procedure was used instead of the actual measurement to
assure an exact correspondence between the helmet liner perforations
and the electrodes attached to the scalp.

Preparation of Electrode Sites

After the four electrode sites were marked, the helmet liner was
removed and each site on the scalp was shaved with an electric trimmer.
The shaved areas were about 1 inch in diameter. A depilatory cream
(Surgex) was applied to the shaved spots and allowed to remain for
20 minutes. The depilatory was removed with a wet tongue blade. Using
4 × 4 inch gauze pads, the electrode sites were washed with Phisohex and
water.

Application of Electrodes

At about 11:30 a.m., the electrodes were applied to the head of
the command pilot in the ready room at Complex 16. The electrode sites
were first scrubbed with a gauze pad containing acetone. Next a high
speed electric drill (Dremel Mototool No. 1) with a sterile dental burr
(No. 6) was lightly touched to the center of each electrode site,
creating a tiny superficial abrasion about 1/16 inch in diameter. The
electrodes, filled with NASA electrolyte paste, were then attached to
the sites with Eastman 910 adhesive. The impedance of each electrode was
then tested with reference to the other three electrodes (in parallel)
using an electrode impedance tester (IMA Electronics, Model ERT-7).
All electrodes were found to have an impedance of less than 1000 ohms.

Preflight Verification of Electrode and Signal Conditioner Operation

Proper operation of electrodes and signal conditioners was verified
by oscillographic writeouts on two different occasions prior to launch.
The first verification was after all biomedical sensors had been applied
and the pilot was wearing only underwear. The second verification was
after the complete space suit was in place. Good quality signals that
were free of electrode artifacts, were obtained on both occasions.

Data Recording Plan

Two channels of a seven-channel tape recorder on board the space-craft were assigned to EEG. One reel of magnetic tape on this recorder is capable of registering 100 hours of data. However, the electrodes last no longer than 4 days; therefore, the recording was programmed to run continuously from shortly before lift-off through the first 100 hours of flight.

Data Recovery

After termination of the Gemini VII flight, the magnetic tape from the Gemini biomedical tape recorder aboard the spacecraft was transcribed onto a standard IRIG format tape (1 inch tape, FM, 1 7/8 ips) by the Manned Spacecraft Center. In the transcription process the "Mac" time code on channel 7 was translated to a standard IRIG "B" time code and recorded on channel 8 of the final tape copy. This copy of the data tape was delivered to our laboratory January 10, 1966.

Writeout of Data

The copy of the data tape was written out for visual interpretation at the Space Neurobiology Laboratory of The Methodist Hospital in Houston, Texas, by using a standard curvilinear ink-writing oscillograph. The tape was played back at 7 1/2 ips (four times the "real-time" speed) onto a chart running at 60 mm/sec to produce a paper writeout equivalent to 15 mm/sec in one-fourth of the actual recording time.

RESULTS

Quantity and Quality of Data Obtained

The electrodes became dislodged from the pilot's scalp before 100 hours had elapsed, but 54 hours and 43 minutes of interpretable EEG data were obtained. Most of the data were of excellent quality from the standpoint of visual interpretation. The bar graph in figure 1 represents data flow of the two EEG channels versus flight time. The bar labeled EEG derivation no. 1 (left central-occiptal, recorded on channel 5 of biomedical recorder) became noisy, probably due to intermittent interruption of electrode contact, after 25 hours and 50 minutes of flight (point B, fig. 1), and no interpretable data appeared in this channel after 28 hours and 50 minutes (point C, fig. 1). EEG derivation no. 2 (midline central-occipital, channel 4 on biomedical tape recorder) gave good, artifact-free data up to 43 hours and 55 minutes (point D,

fig. 1), at which time it became intermittently noisy; no interpretable data was recorded in this channel after 54 hours and 28 minutes of flight (point E, fig. 1).

Also indicated on figure 1 are the two sleep periods which occurred during the recording (shaded areas), meals (black squares), and one period during which the subject closed his eyes for 1 hour without falling to sleep (probably an unsuccessful attempt to sleep). The sleep periods will be analyzed in the section of the text that is titled "Analysis of the Sleep Periods." The meals are indicated because they represent a temporary interruption in the interpretability of the EEG data due to artifacts produced by rhythmic chewing motions (see fig. 6).

EEG Pattern in the Waking State

The astronaut was alert and active during the major part (77.5%) of the recording. The EEG pattern under these circumstances shows a mixture of artifacts and low voltage cerebral potentials, which are difficult to interpret by visual methods. Figure 2 shows the 50 microvolt calibration wave shapes and examples of the EEG pattern in the active waking state are shown in figures 3, 4, and 5.

Figure 3 is a recording prior to first-stage ignition, and the record consists of occasional runs of low voltage alpha rhythm superimposed upon a somewhat unsteady baseline and mixed with frequent transient down-going deflections, which are eye-blink potentials. Occasional runs of low voltage between 5 and 7 cycles per second activity appear in the record. These recordings may be runs of theta activity but are difficult to distinguish from rapid ocular artifacts.

Figure 4 is a recording during ascent and is essentially the same as the recording prior to lift-off, but in addition, continuous muscle potentials are superimposed upon the trace.

Figure 5 is a section of the record after 24 hours in orbit which shows a more relaxed pattern with much more rhythmic alpha rhythm and less muscle potentials. The burst of high voltage alpha activity on the left side of this recording probably corresponds to a period when the astronaut briefly closed his eyes. Clear examples of down-going eye-blink potentials are at about 1-second intervals in the right-hand part of the trace.

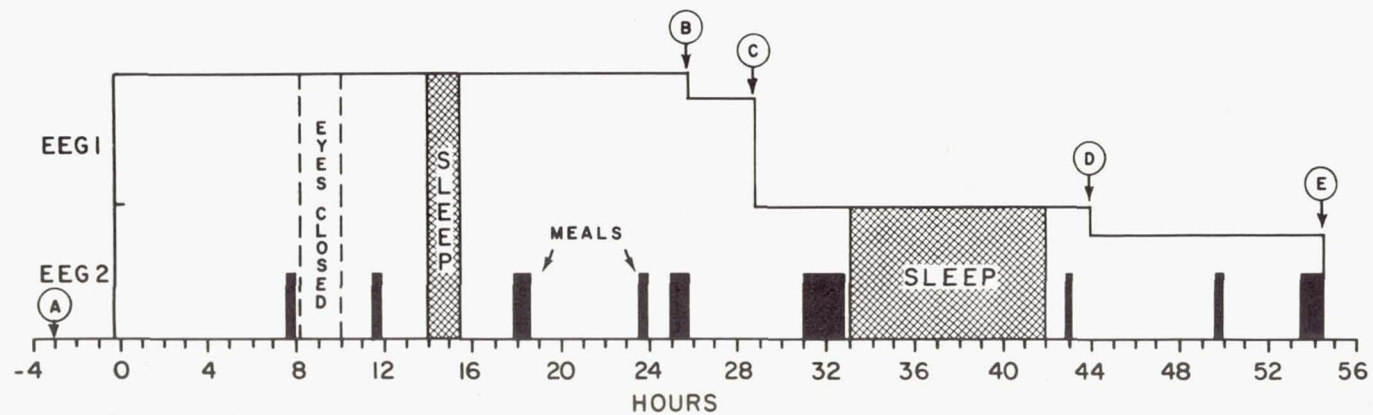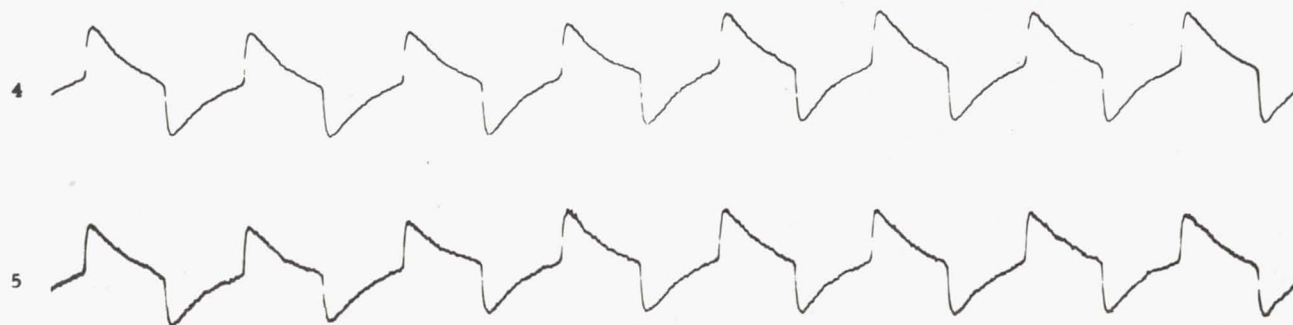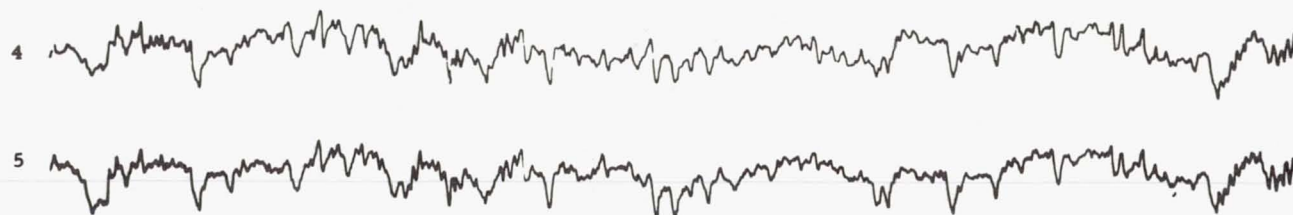Figure 1. – Data flow of the two EEG channels versus flight time.

CALIBRATION: 50 microvolt square waves, 0.5 cps

Figure 2. - Square wave shapes used for calibration.

BEFORE LIFT OFF: minus 10 min.

Figure 3. - EEG pattern at T-10 minutes.
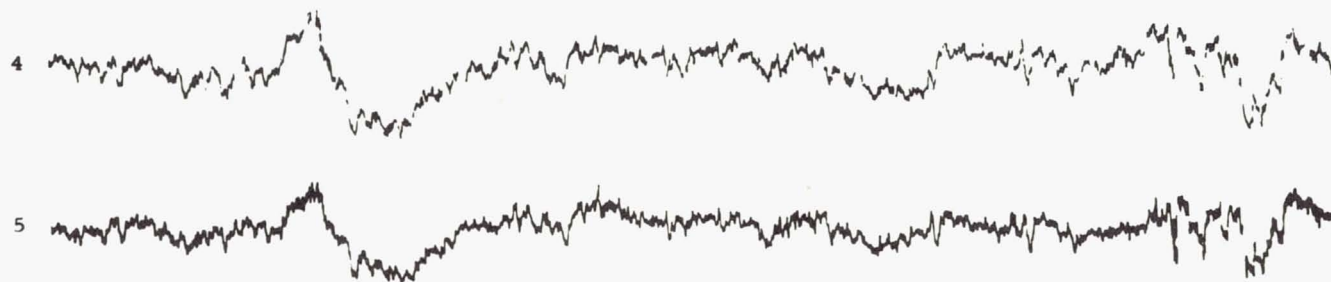
DURING ASCENT: plus 5 min.

Figure 4. - Recording during ascent.
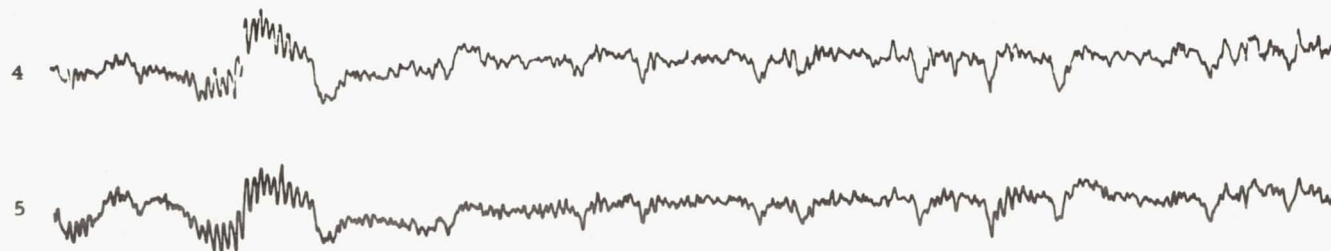
IN ORBIT: 24 hr., 27 min.

Figure 5. - Section of the record after 24 hours in orbit.

During meals, rhythmic slow potentials between 1.5 and 2 cycles per second mixed with muscle potentials obscure EEG activity and is illustrated on figure 6. These artifacts are produced by rhythmic chewing motions.

When the astronaut closed his eyes (see fig. 7), the record shows a strong alpha rhythm, is of good quality, and free of artifacts. Figure 7 is a sample of the record during a 2-hour period (8:12 to 10:19 flight time of the first day) when the astronaut apparently tried to sleep but was unable to sleep.

By visual inspection of the record during the waking state, there seems to be slightly more theta (4 to 7 cycles per second) activity in the record than was observed in this subject prior to flight, but this is a subjective impression and can only be evaluated accurately by electronic means. From the standpoint of visual interpretation of the record, the following conclusions can be made:

1. No gross pathological changes occurred during flight, either during launch or in orbit.

2. Any changes due to stress or weighlessness present in the record are minor and cannot be detected by conventional visual analysis.

Analysis of the Sleep Periods

As indicated previously on figure 1, two sleep periods occurred during the recording. The first sleep period occurred at 14:07 hours (flight time) and lasted 1 hour and 28 minutes. The second sleep period began at 33:10 hours and lasted 8 hours and 46 minutes.

The EEG patterns during sleep are very distinctive, and because the subject is quiet, no artifact obscures the record. The records obtained during sleep in this experiment were of good quality and are shown on figures 8, 9, 10, 11, 12, 13, and 14. These samples of the recording illustrate the EEG characteristics at various stages or levels of sleep which are used to plot the overall sleep pattern. Stage 0 consists of a full alpha rhythm and is the resting, eyes-closed pattern. In the transition from stage 0 to stage 1 sleep (figs. 8 and 9), the alpha rhythm decreased in voltage and is gradually replaced by a low voltage theta rhythm, which is the first sign of drowsiness. Stage 2 sleep, or light sleep, is characterized by moderately high voltage rhythmic or semi-rythmic theta activity and sharp transient waves of negative polarity originating from the vertex region (see fig. 10).
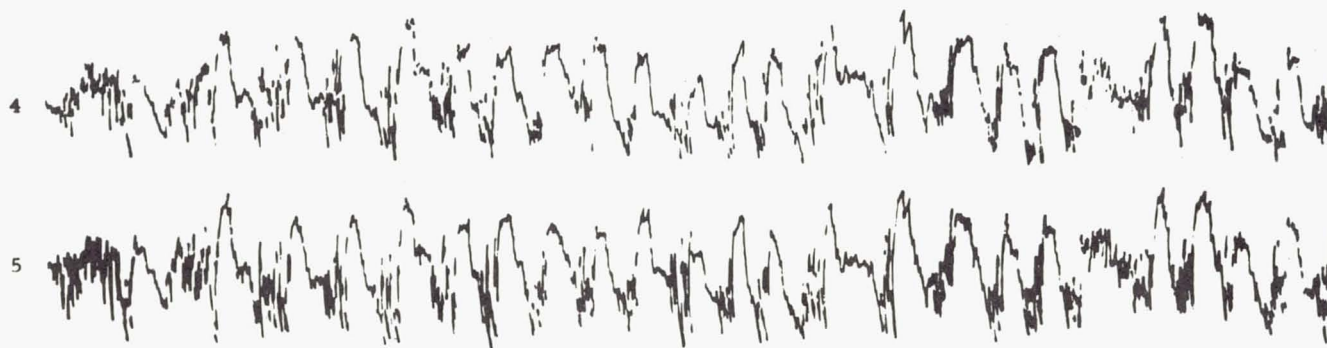
DURING MEAL: 7 hr., 49 min.

Figure 6. - Rhythmic slow potentials between 1.5 and 2 cycles per second mixed with muscle potentials.

RESTING, EYES CLOSED: 8 hr., 16 min.

Figure 7. - Record showing a strong alpha rhythm.

TRANSITION TO STAGE 1 SLEEP: 33 hr., 17 min.

Figure 8. - Alpha rhythm decreasing.

STAGE 1 SLEEP (continuation of above): 33 hr., 17 min.

Figure 9. - Low voltage theta rhythm.

STAGE 2 SLEEP: 33 hr., 24 min.

Figure 10. - Moderately high voltage rhythmic or semi-rhythmic theta activity.

Stage 3 sleep, or moderate sleep (see fig. 11) is characterized by sleep "spindles", or sigma activity (14 cps), mixed with vertex transients and low-voltage delta activity (between 1 and 3 cps). At this stage and in late stage 2 there is also some monophasic (positive) theta activity in the occipital region. Stage 4 sleep, or deep sleep, is characterized by continuous high-voltage delta activity (see fig. 12). When the subject is aroused from sleep (fig. 13), the record returns quickly to stage 0, or the resting pattern.

The recently-described paradoxical phase of sleep is difficult to recognize without the records of eye movement because the pattern is similar to stage 1 sleep. The sample on figure 14, which resembles a mixture of stage 1 and stage 2 sleep, shows some of the characteristics that have been previously observed in individuals during paradoxical sleep with rapid eye movements - runs of three per second saw-tooth-shaped waves, runs of low voltage alpha and theta activity, low voltage beta activity without spindles, and occasional slow transients having a period of about 1 second. This type of pattern, which might represent paradoxical sleep, occurred for two fairly long sections during sleep period no. 2 - at 11:05 hours and 14:20 hours.

The sleep periods on the recording were visually scanned and each minute of record was classified as to the level or stage of sleep according to the preceding criteria. The EEG stage of sleep for each 1-minute epoch of sleep is shown in graphic form in figure 15. The uppermost level on the vertical axis represents the eyes-open, alert-type pattern. The next level is the eyes-closed, resting pattern, or stage 0. The heavy horizontal line in the center of stage 0 represents the division between waking patterns and sleep patterns. The next four levels represent the four stages of sleep in order from light sleep down to deep sleep. When, as often happened, more than one EEG stage of sleep was seen in a 1-minute epoch, the vertical line indicating stage of sleep overlaps the two or more stages seen during that minute. The horizontal axis of these graphs is flight time in hours and minutes, translated from the "Mac" time code on the tape. In addition to the two sleep periods during flight, a similar analysis was made of the control sleep period made in our laboratory during September of 1965 (upper left graph in fig. 15). This information is given to compare rates of falling to sleep, but it cannot be used for pattern of sleep period since the subject was awakened before spontaneous sleep was completed.

The graph of EEG sleep levels shows that sleep period no. 1 was primarily light sleep in addition to being very brief. Sleep period no. 2, however, appears to be quite adequate in terms of depth and length of sleep. There were three sections, totaling about 75 minutes, during which the pilot remained in an uninterrupted deep sleep. No such continuous stage 4 sleep was observed in the control sleep period or in
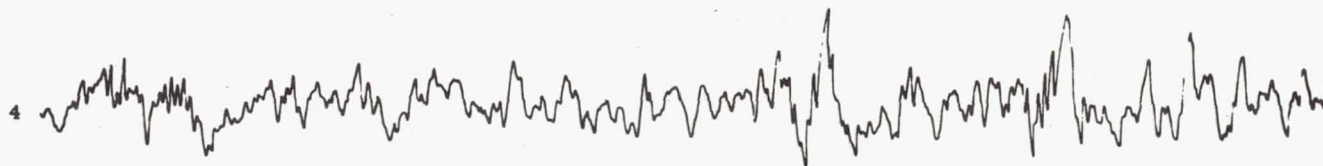
STAGE 3 SLEEP: 34 hr., 16 min.

Figure 11. - Sigma activity mixed with vertex transients and low-voltage delta activity.
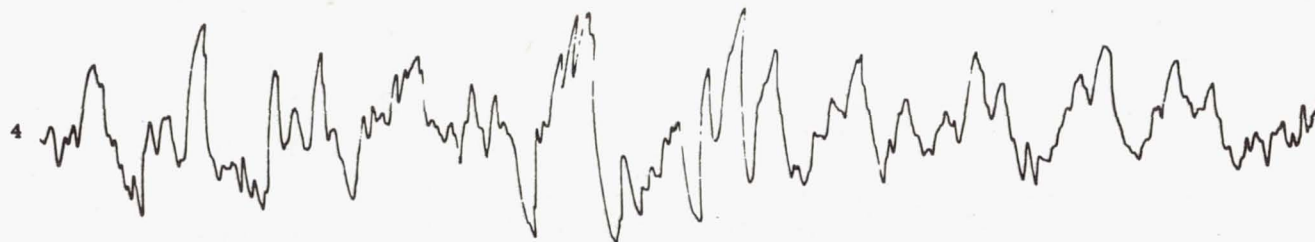
STAGE 4 SLEEP: 34 hr., 44 min.

Figure 12. - Continuous high-voltage delta activity.
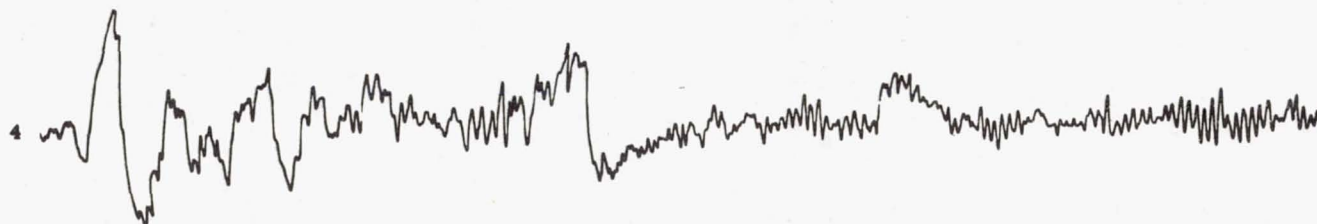
PARTIAL AROUSAL: 36 hr., 53 min.

Figure 13. - Partial arousal.

STAGE 1-2 SLEEP: 35 hr., 11 min.

STAGE 1-2 SLEEP (continued): 35 hr., 11 min.

Figure 14. - Characteristics of paradoxical sleep.

sleep period no. 1. This increase in depth of sleep during the second period is probably a result of several factors, including inadequate sleep in the first period and accommodation of the pilot to the novel conditions of space flight.

The cyclic variations in level of sleep during period no. 2 are typical of sleep patterns observed on earth. Figure 16 shows the cyclic pattern reported by Dement and Kleitman[1] in their studies of normal sleep. It should be noted, however, that the astronaut aroused to an alert stage of EEG activity much more often than did the subjects in Dement and Kleitman's study. (Fig. 16 shows only one arousal to the alert state and that occurred at 5 1/2 hours.) Of all minutes of sleep during flight, 26.4% showed some EEG activity of the type seen in the alert state. To search for factors that might correlate with the arousals in the astronaut's sleep pattern, all spacecraft environmental factors will be considered; these factor are cabin temperature variations, pressure changes, lighting factor, etc. So far, only data on lighting has been obtained. Although the windows of the spacecraft were arranged to exclude sunlight during sleep periods, there is a suggestive relationship between sunlight and arousals from sleep: 35.2% of the minutes spent in sunlight contained arousal EEG activity, whereas only 9.3% of the minutes spent in the earth's shadow contained arousals.

RECOMMENDATIONS

From the experience gained in this first attempt to record EEG during space flight, the following recommendations are made with the aim of enhancing the value of future attempts:

1. Baseline studies should be more comprehensive and include one or more sleep periods of normal length.

2. Electrodes should be more securely fastened, or else they should be of a type which could be reapplied by the astronaut in flight when they become dislodged. In this regard, a protective cap might be worn by the subject after removal of space suit helmet in order to protect the electrode application.

3. Efforts should be made to include a recording during reentry and recovery phases of the flight.

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[1] Dement and Kleitman, Electroenceph. Clin. Neurophysiol. 9:673, 1957.
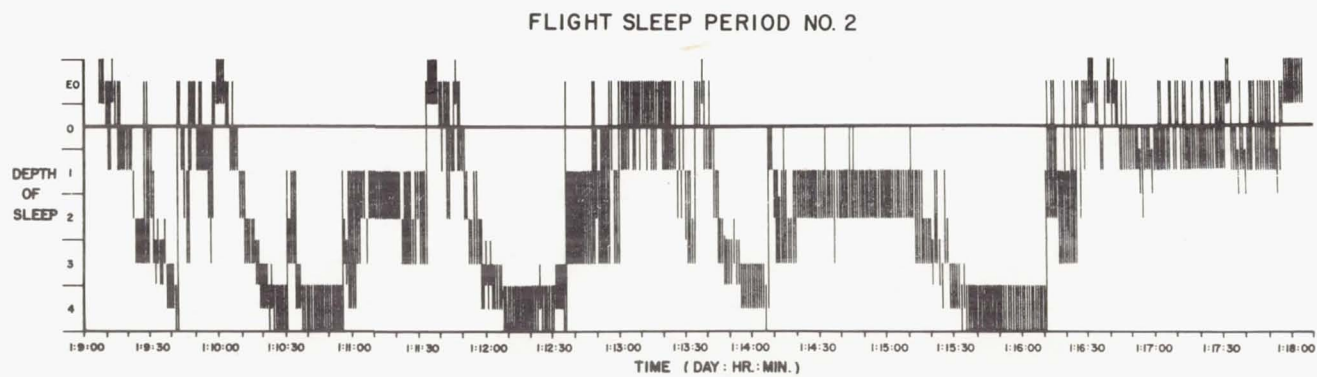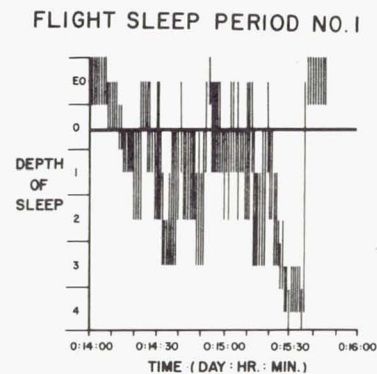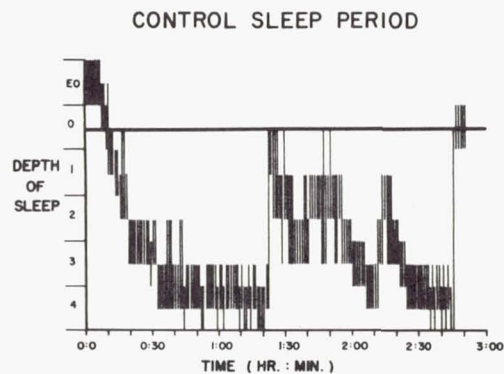
Figure 15. - The EEG stage of sleep for each 1-minute epoch of sleep.
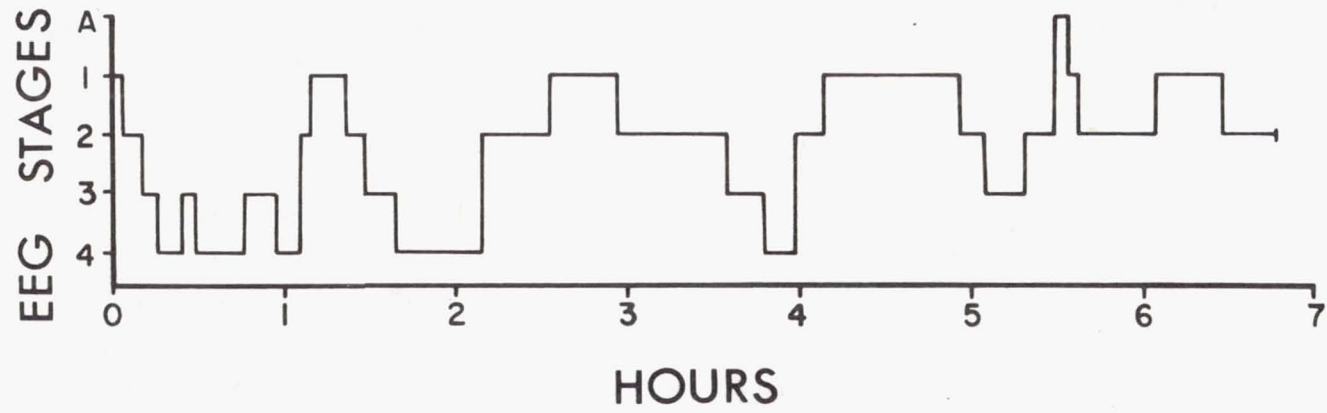
Figure 16. - Cyclic pattern reported by Dement and Kleitman.

EXPERIMENT M-9, GEMINI HUMAN OTOLITH FUNCTION

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One program now in progress with the goal of determining the effects of space flight on vestibular function and spatial orientation will be described. The program is entitled, "Medical Experiment M-9, Human Otolith Function," and is being conducted through the Space Medicine Branch by Dr. Ashton Graybiel and Dr. Earl Miller, of the U.S. Naval Aerospace Medical Institute, Pensacola, Florida. Because the data analysis has not been completed, only the general procedures and equipment will be discussed herein.

Two parameters are being examined, the ocular counterrolling reflex and the egocentric visual localization of horizontal.

The counterrolling reflex occurs when the head is tilted away from vertical or when some other adequate stimulus is applied to the otolith organ. In addition to postural muscular responses, the extrinsic ocular muscles cause the eyeballs to rotate about their optical axes in a direction opposite from the direction of body tilt. In man, the normal magnitude of this response is about 6° when the body is tilted 60° from vertical. The implication of the otolith organ in this response is demonstrated when labyrinthine defective subjects are tested and no counterrolling is observed.

Figure 1 shows the counterrolling tilt device. The subject wears a Velcro vest tightly applied and is strapped firmly in the stretcher-like portion with most of his body weight resting on a saddle. The device maintains a constant head-to-body relationship even when tilted to 90° from the vertical.

Figure 2 shows details of the photographic method for recording the counterrolling response, a flash gun, a red fixation ring to control voluntary eye movements, and a camera. The axis of rotation, the optical axis of the eye, and the axis of the camera are identical. The head is fixed by means of a custom fitted biteboard. Films obtained at tilt positions are enlarged approximately 300 times and superimposed on films taken in the upright position to determine the magnitude of the response. Accuracy is within several minutes of arc.
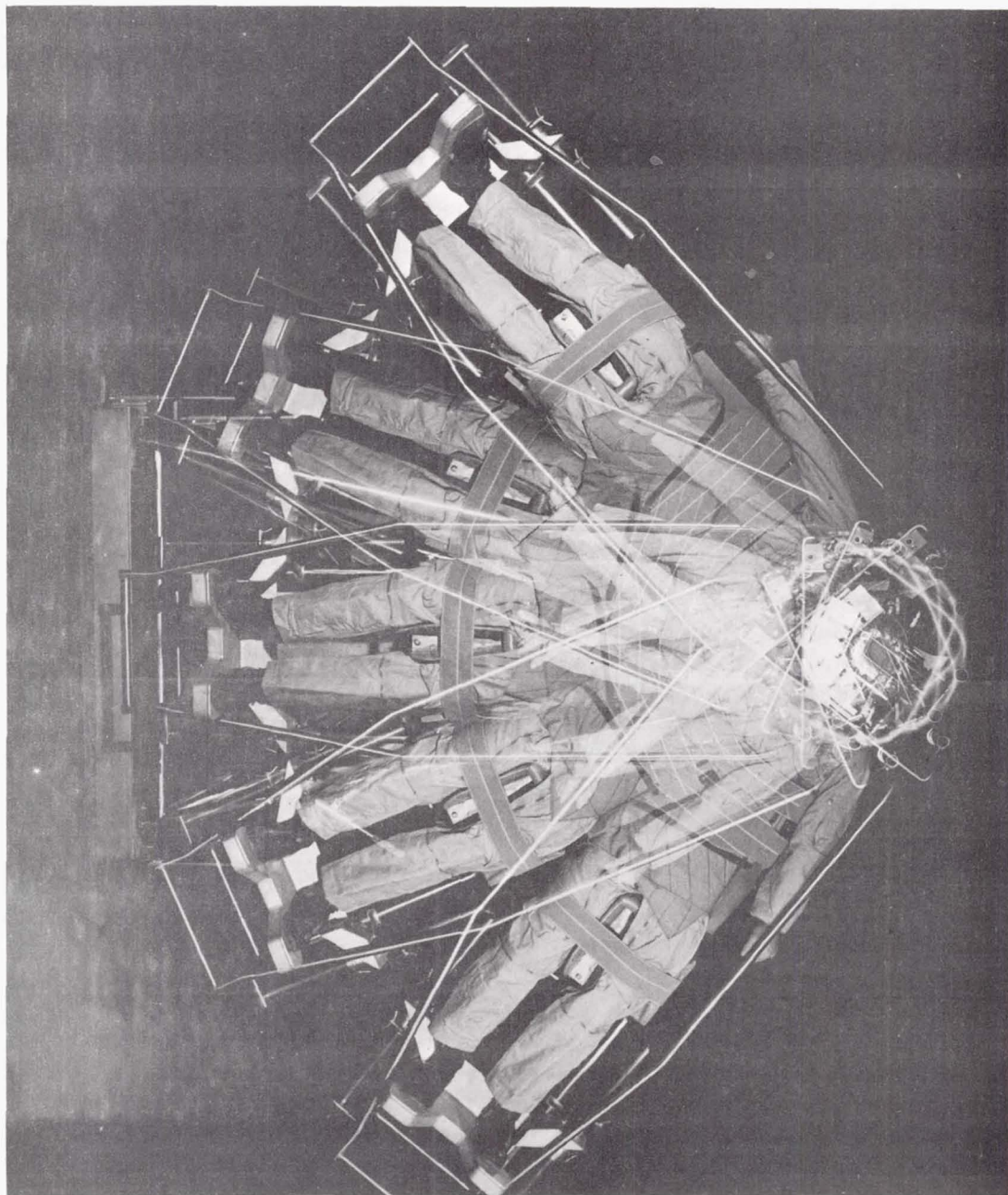
Figure 1

GEMINI MEDICAL EXPERIMENT M-9
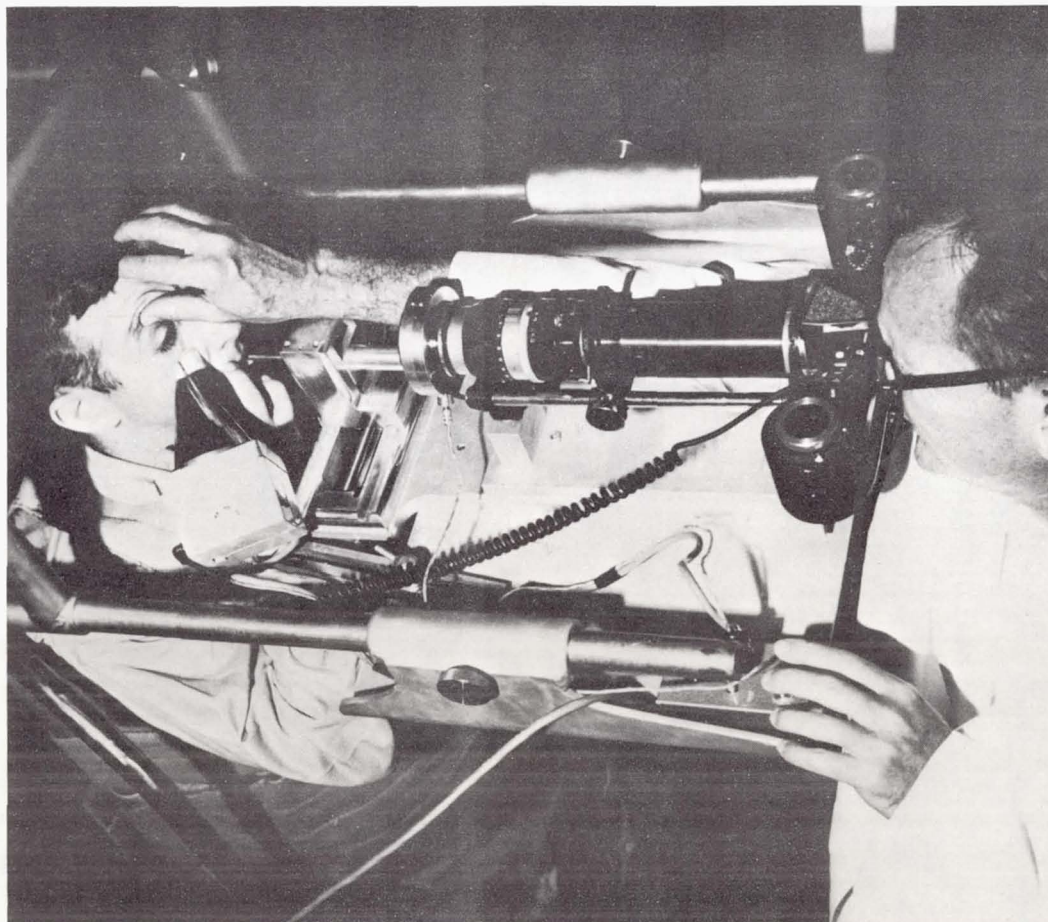
Figure 2

The second parameter being investigated, the egocentric visual localization of horizontal (EVL), may best be described by an example: If an observer regards a dimly luminous line in darkness while seated upright during ordinary gravitational conditions, he is able to adjust the line to horizontal with great accuracy. If he is now exposed to a change in the gravito-inertial vertical, such as by centrifugation, he has the illusion of being tilted and when instructed to set the line to horizontal, adjusts it with great accuracy perpendicular to the resultant of earth gravity and the centrifugal force. This indicates that in the absence of visual cues (the line itself being an inadequate cue) the ability of the subject to estimate vertical and horizontal is under the influence of gravitational cues, that is, otolithic plus secondary somatic cues such as sensations from the seat of the pants, muscles, and joints, et cetera. The otolith seems to be of primary importance in this response also since naive, labyrinthine defective persons are quite inaccurate in this task as well as when they are tilted into various positions in the counterrolling device and required to make this judgment of horizontality.

Figure 3 shows the flight instrument used to measure EVL. It is fixed to the subject by means of a biteboard not shown here. The subject looks into the instrument and sees a luminous line against a black background. The line can be adjusted about 360° by means of a knurled dial; a vernier scale allows another crewmember to read off the subject's setting.

Figure 4 shows the vision tester being used in a spacecraft simulator. The bracket fixes the instrument as well as the subject's head with respect to the roll axis of the spacecraft.

Figure 5 shows Frank Borman using the EVL instrument during the Gemini VII flight.

Some of the questions to which the M-9 experiment was directed are: Does the sensitivity of the otolith apparatus change during long periods of weightlessness during which its normal stimulus is absent? If there are changes, will illusions of being tilted or motion sickness result? Are somatic cues sufficient for maintaining orientation with respect to the spacecraft in the absence of visual and otolithic cues? Will the otolithic end organs remain quiescent during zero gravity, or will some type of abnormal input to the CNS occur? If so, will adaptation or learning occur during the flight? Will the effects of suddenly submitting the otolith apparatus to the forces of reentry prove incapacitating?

Briefly, the procedure for M-9 was to measure counterrolling and EVL on prime and backup crews for Gemini V and VII on several occasions

MEDICAL EXPERIMENT M-9
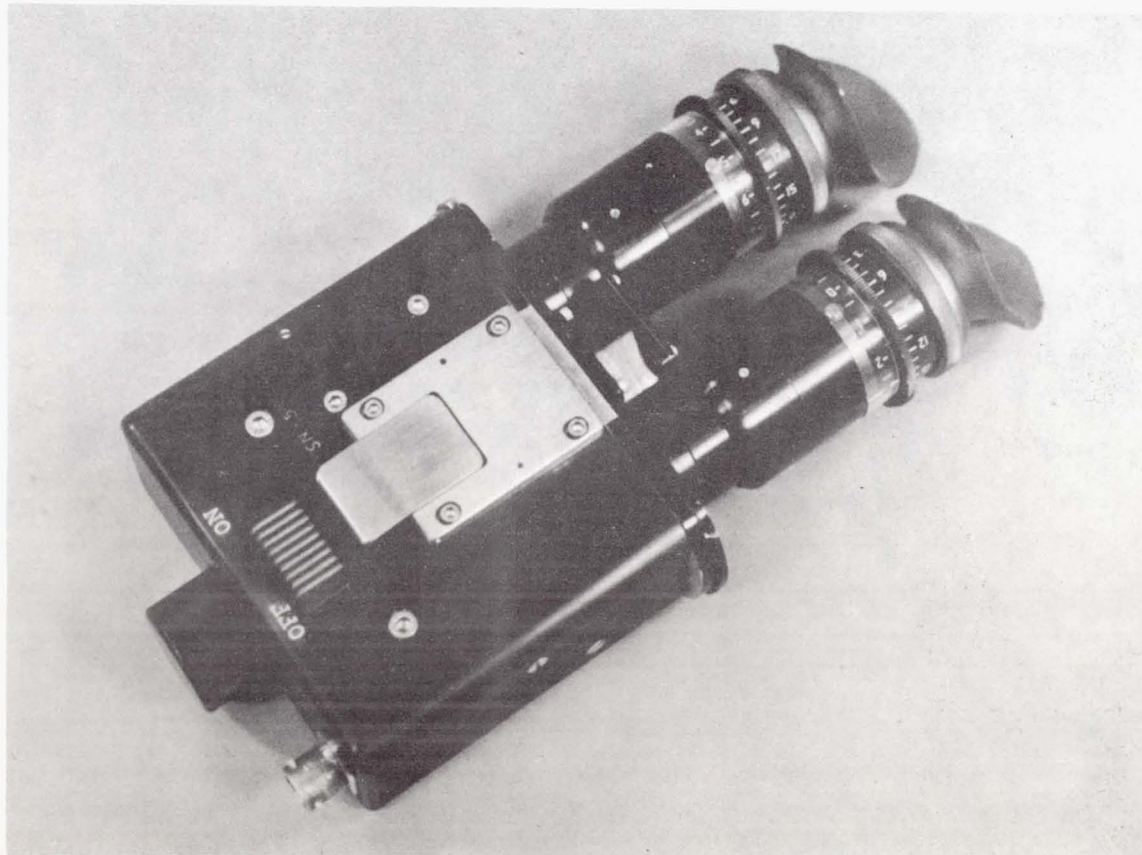
Figure 3

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MEDICAL EXPERIMENT M-9
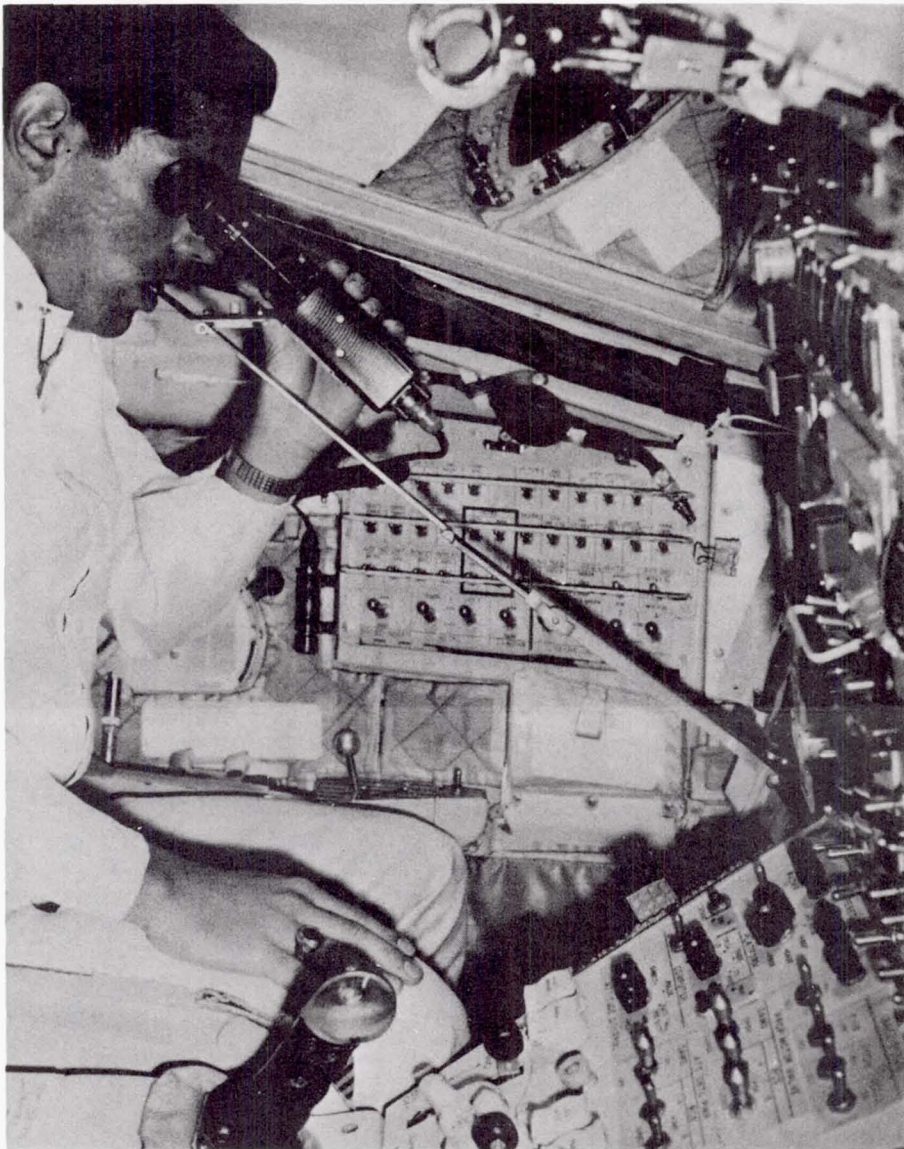
Figure 4

MEDICAL EXPERIMENT M-9
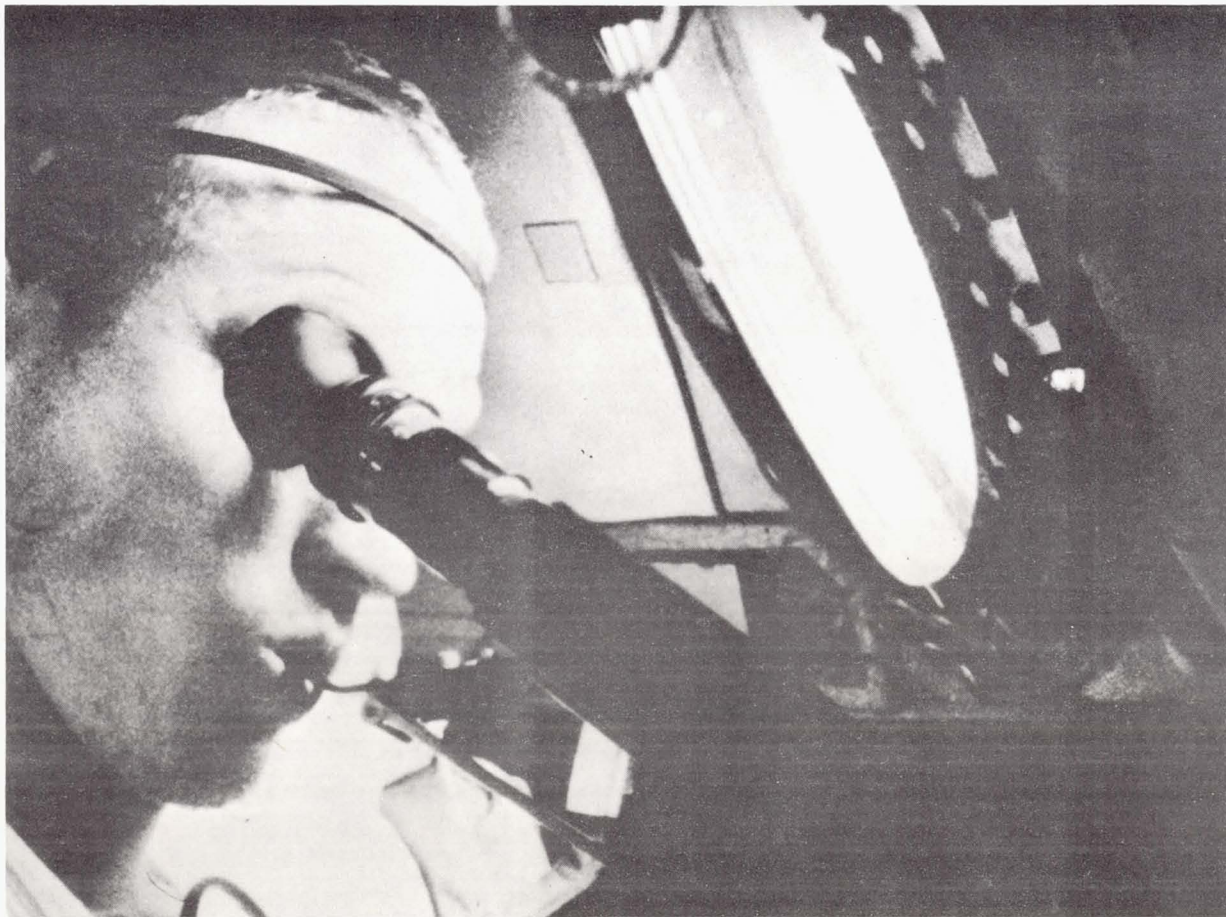
Figure 5

preflight, and postflight as soon as possible after recovery. The EVL was measured by each man daily <u>during</u> the flight. The apparatus in its present size does not permit the measurement of counterrolling within the confines of the small spacecraft, hence, our limitation to preflight and postflight measurements. The data obtained in this manner are now being compared with that collected from an ongoing series of tests on other test pilots, other astronauts, labyrinthine defective subjects, persons selected for their experience of high g forces on centrifuges, persons tested in water immersion studies, subjects tested under transitory zero g in parabolic aircraft flights, and a large number of randomly selected normals.

Figure 6 shows a prototype of an instrument which will be used on manned Apollo flights to record essentially the same type of data with the addition of a feature enabling measurement of subjective height above horizon.

MEDICAL EXPERIMENT M-9A

Figure 6

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EFFECTS OF MITRAL STENOSIS AND ATRIAL FIBRILLATION

UPON SODIUM EXCRETION

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Retention of sodium has been recognized as one of the cardinal pathophysiologic processes underlying the retention of water, which characterizes congestive heart failure. The mechanism of sodium retention in patients with heart disease, however, remains incompletely understood. The work of Gauer and Henry raised the possibility that congestive heart failure, chronic over-distention of the left atrium may alter reactivity of volume receptors and reduce excretion of sodium and water. Sharpey-Schaefer and others have suggested that decreased atrial pulsations may decrease the stimulation of volume receptors and, thus, congestive heart failure may result from retention of sodium and water.

The studies to be reported in this paper were conducted to determine whether alterations in atrial function would alter the excretion of sodium load. Patients with mitral stenosis were chosen as subjects because, clinically, this disease is known to be associated with a tendency towards fluid retention.

MATERIAL AND METHODS

One normal subject (a 35-year-old man) and six ambulatory patients having mitral stenosis (five women and one man with a mean age of 50.3 years) were studied while they were patients in a metabolic ward. All patients were characterized hemodynamically by right and left heart catheterization. The severity of mitral stenosis ranged from mild (mitral valve area 1.4 cm^2) to severe (mitral valve area 0.5 cm^2) and the clinical classification ranged from class I to class IV. All but one patient, initially, were in atrial fibrillation.

The patients were placed on a diet containing 25 or 50 mEq sodium, constant in potassium and calories. When balance had been reached, an

infusion of 308 mEq sodium in 2 liters of water was given over 2 hours. Four patients with mitral stenosis and atrial fibrillation were cardio- verted to regular sinus rhythm and their response to the same sodium load was reevaluated on days 0 to 7. One of these patients was re- studied 1 month after operative repair of mitral stenosis, but again in atrial fibrillation. Of three patients studied in atrial fibrillation and after conversion, cardiac output was measured for both states.

RESULTS

Figure 1 presents the cumulative excretion of sodium during the first 3 days after the sodium load in the normal subject, the patient with mitral stenosis and normal sinus rhythm, and the five patients with mitral stenosis and atrial fibrillation. Excretion of sodium was rapid and complete in the normal subject as well as in the patient with mitral stenosis and normal sinus rhythm. In contrast, all patients with mitral stenosis and atrial fibrillation showed delayed and incom- plete excretion of the sodium load.

Figure 2 presents the detailed balance data of a 58-year-old lady with mild mitral stenosis (mitral valve area 1.4 cm^2) atrial fibrilla- tion, in class II, on a 25 mEq sodium diet. A good part of the first sodium load is retained; however, after conversion to regular sinus rhythm, sodium is excreted more completely.

On figure 3, this is shown in terms of excretion of sodium ex- pressed in percent of sodium load. For 3 days, only 31 percent of the load was excreted when the patient was in atrial fibrillation; of the load given on the day of conversion to regular sinus rhythm, 79 percent was excreted in 3 days. When another load was given 7 days after con- version, 69 percent was excreted in 3 days.

The effect of conversion to normal sinus rhythm upon the cumulative 3-day excretion of the sodium load for the entire group of four patients so studied is shown on figure 4. The increase from a mean excretion of 50.4 percent in atrial fibrillation to 72.3 percent in normal sinus rhythm is significant at the 5 percent level, but note, however, that sodium excretion did not become normal.

The quantitative responses to the initial sodium load were analyzed in relation to clinical and physiological parameters. No relationship could be demonstrated between sodium excretion and severity of the stenosis, left atrial pressure, systemic pressure, heart rate, cardiac output, left atrial size, clinical classification, or digitalis status.
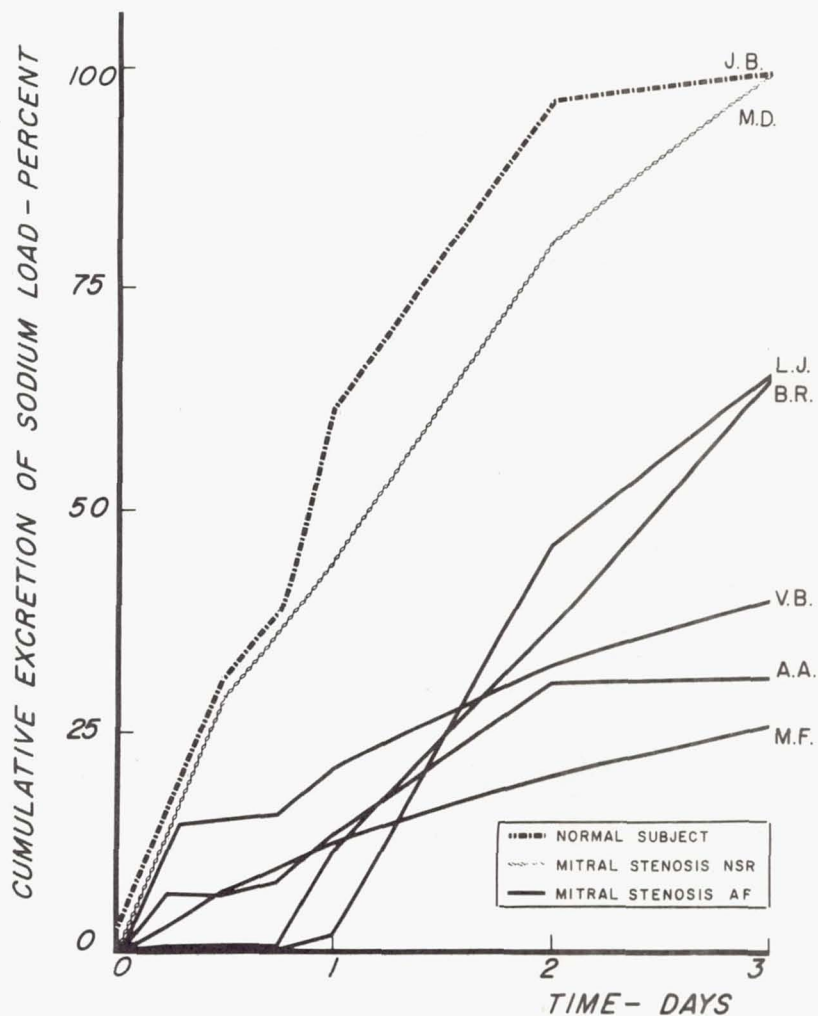
Figure 1.- The cumulative excretion of a sodium load of 308 mEq in a normal subject, a patient with mitral stenosis and normal sinus rhythm, and 5 patients with mitral stenosis and atrial fibrillation.
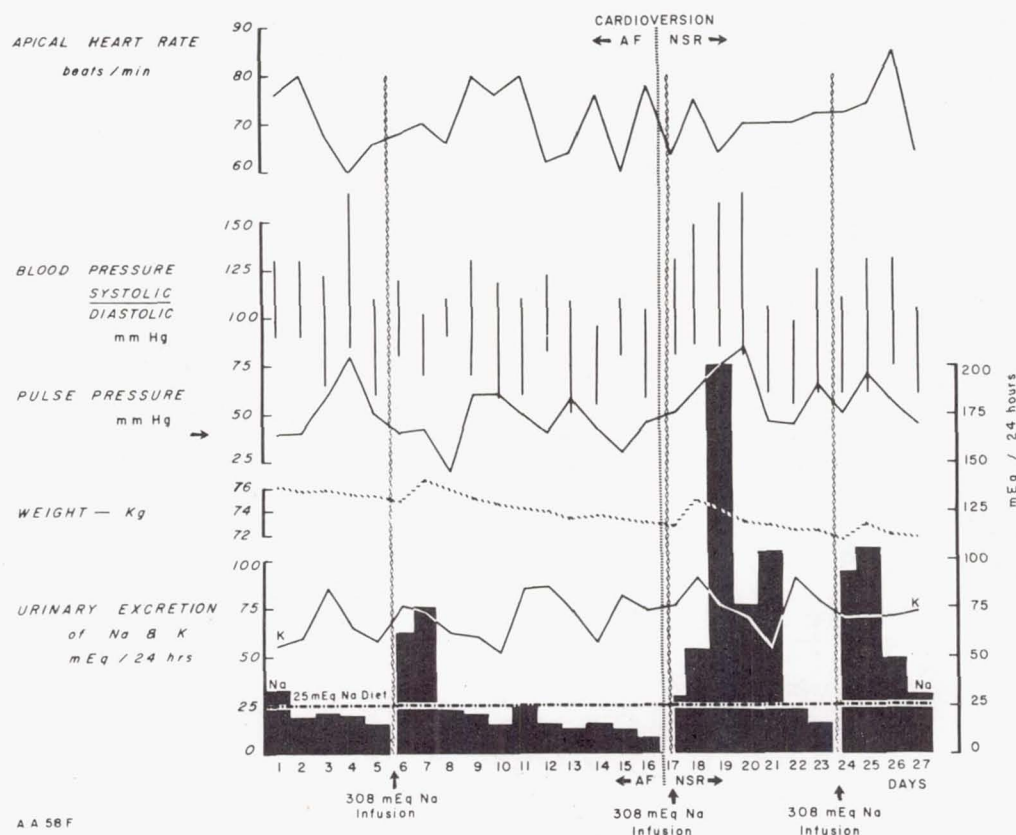
Figure 2.- Balance study of a 58-year-old woman with mild mitral
stenosis (mitral valve area 1.4 cm^2), atrial fibrillation,
class II, given a sodium load on day 6, converted to normal
sinus rhythm on day 17, given a second sodium load on day 17,
and given a third sodium load on day 24, still in normal sinus
rhythm.
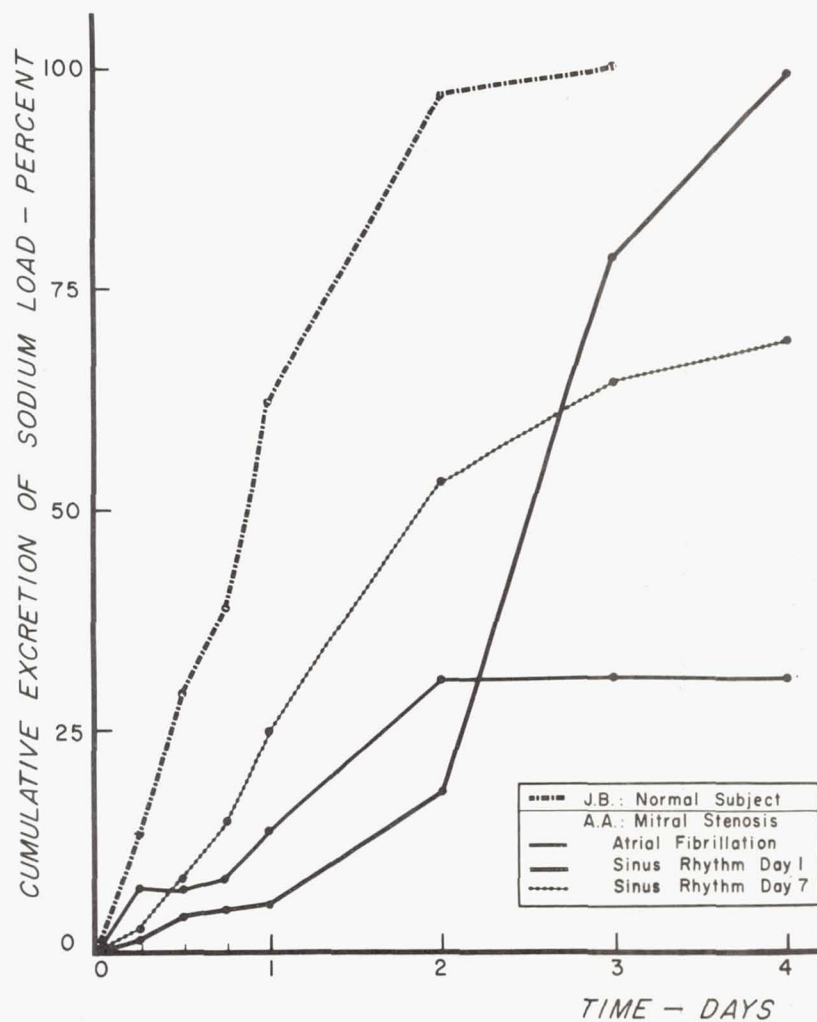
Figure 3.- The cumulative excretion of a standard sodium load in a
58-year-old woman with mild mitral stenosis in atrial fibrilla-
tion, early after cardioversion to normal sinus rhythm, and
1 week later. The detailed data of this study are depicted in
figure 2.
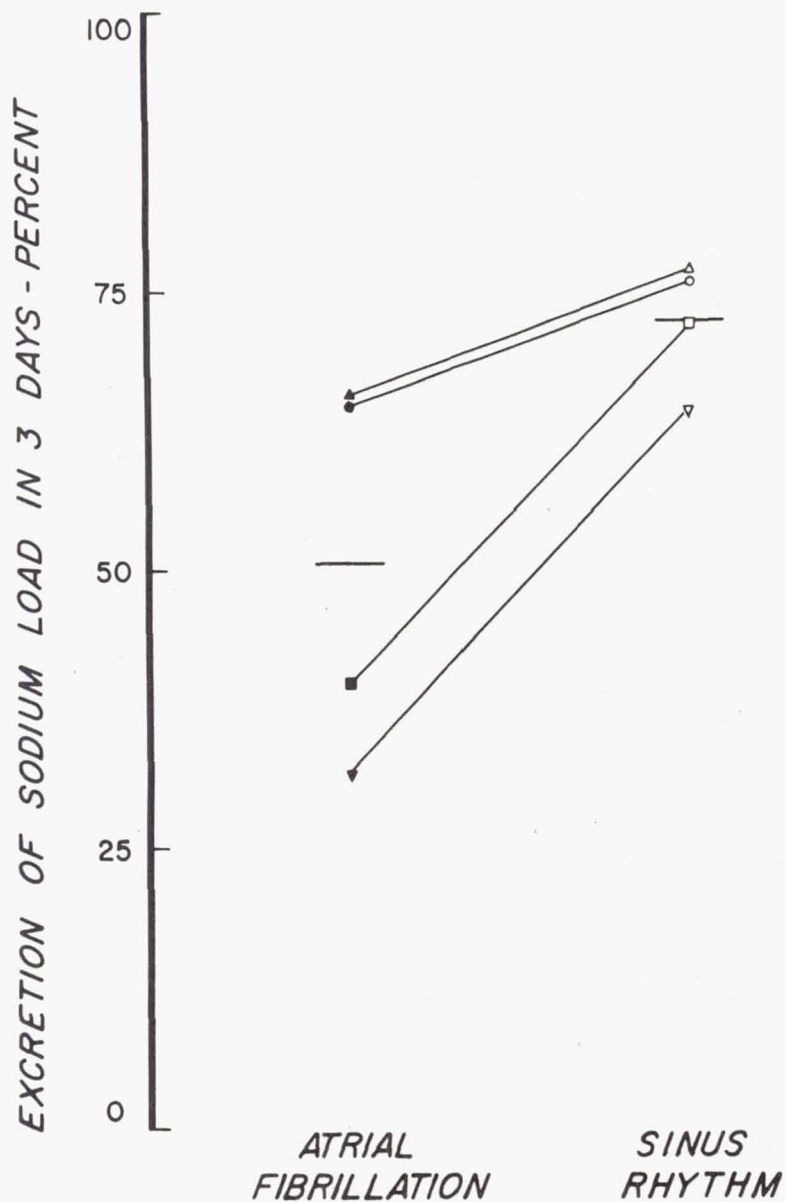
Figure 4.- The effect of conversion to normal sinus rhythm upon
the cumulative 3-day excretion of a standard sodium load by
4 patients with mitral stenosis and atrial fibrillation.
The mean excretion increased from 50.4 percent to 72.3 per-
cent (p < 0.05).

On the three patients studied hemodynamically both before and after conversion, cardiac output increased by 12 percent in one, by 8 percent in another, and did not change in the third, while mean arterial pressure decreased in all on the average by 7 percent.

One patient was restudied after successful surgical repair of mitral stenosis. As shown on figure 5, excretion of the sodium load became essentially normal although atrial fibrillation persisted.

COMMENTS

The data presented indicates of the patients studied that the combination of mitral stenosis and atrial fibrillation were always associated with delayed and incomplete excretion of a sodium load. After conversion to normal sinus rhythm, the rate of excretion of the sodium load was significantly increased, although it remained abnormally low in these patients who still had mitral stenosis. However, surgical correction of severe mitral stenosis in one patient normalized excretion of the sodium load, notwithstanding persistence of atrial fibrillation.

Thus, in patients with mitral stenosis, the obstruction at the mitral valve and atrial fibrillation may constitute separate determinants of the response to a sodium load, each capable of favoring retention of sodium, and each reinforcing the other.

Both mitral stenosis and atrial fibrillation are known to limit or decrease cardiac output and, presumably, glomerular filtration rate; this is not a consistent effect, especially not if the ventricular response to atrial fibrillation is slow. However, both mitral stenosis and atrial fibrillation are also associated with altered left atrial size and function. The mediation of the effect of mitral obstruction and of atrial fibrillation upon excretion of a sodium load remains to be elucidated.
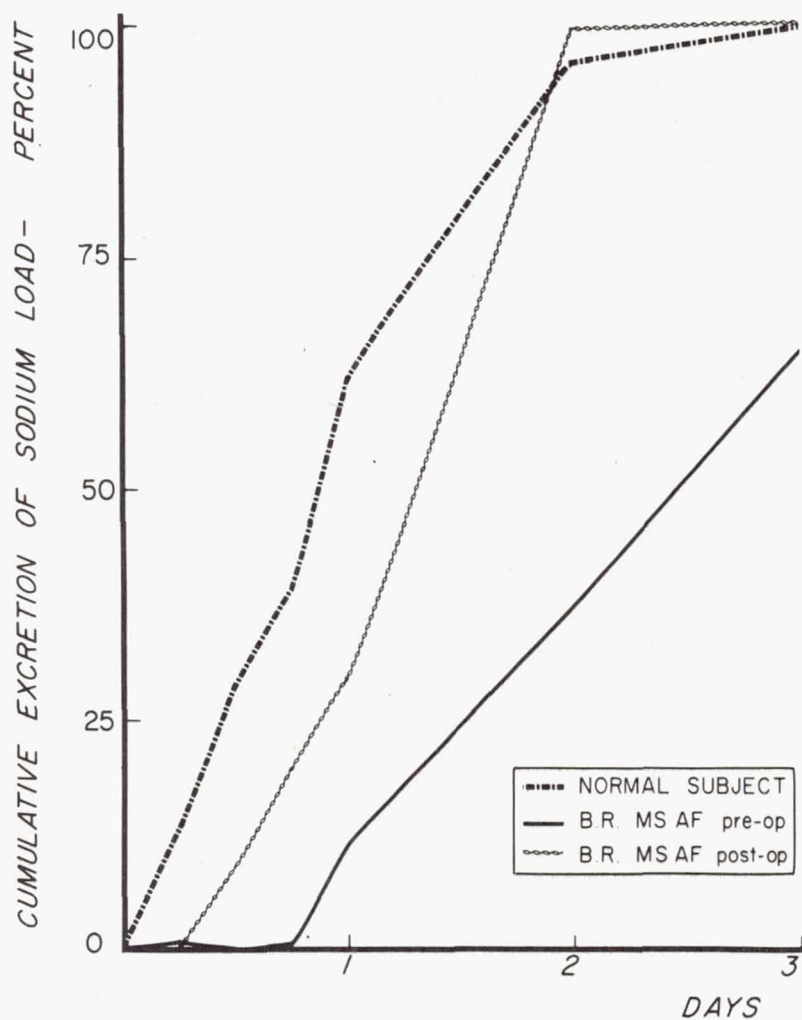
Figure 5.- Effect of mitral valvuloplasty upon the cumulative 3-day
excretion of a standard sodium load by a 61-year-old woman with
mitral stenosis and atrial fibrillation.

HEMODYNAMIC INFLUENCES ON TUBULAR REABSORPTION AND SODIUM EXCRETION

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Last year it was reported that in the dog, changes in tubular reabsorption of sodium and sodium excretion may relate in some way to changes in renal blood flow. Thus, infusions of isotonic saline may increase renal blood flow and sodium excretion independently of changes in glomerular filtration or the effect of adrenal salt-retaining steroids; an example of this is illustrated on figure 1. In this and similar studies the infusion of saline was associated with increased excretion of sodium without increased filtered sodium as renal blood flow increased. The extraction ratio for para-aminohippurate is decreased during saline loading, suggesting a proportionately greater increase in "non cortical" renal plasma flow. This relationship between renal hemodynamics and the regulation of sodium excretion has been investigated further to determine whether hemodynamic factors may bring about changes in sodium excretion in the absence of expansion of the extracellular compartment.

In one series of studies, anesthetized animals receiving an exogenous mineralocorticoid underwent unilateral renal vasodilatation by the infusion of acetylcholine into one renal artery; a representative study is illustrated on figure 2. The infusion of acetylcholine resulted in a large increase in renal blood flow, and there was an associated increase in sodium excretion. This increased excretion of sodium was not accompanied by increased glomerular filtration, and thus represents decreased tubular reabsorption of sodium. When the infusion of acetylcholine was discontinued renal blood flow and sodium excretion returned to control rates. Blood flow and sodium excretion were not increased in contralateral control kidneys.

In another series of studies the effect of combined renal vasodilatation and increased arterial pressure have been investigated and a summary of these experiments is shown on figure 3. On the left are represented the experimental vasodilated kidneys, and on the right are shown the results from contralateral control kidneys of the same animals. Renal vasodilatation alone, the center column, increased renal plasma flow and sodium excretion in all studies, but glomerular filtration was not increased in more than half the observations. Hemodynamics and
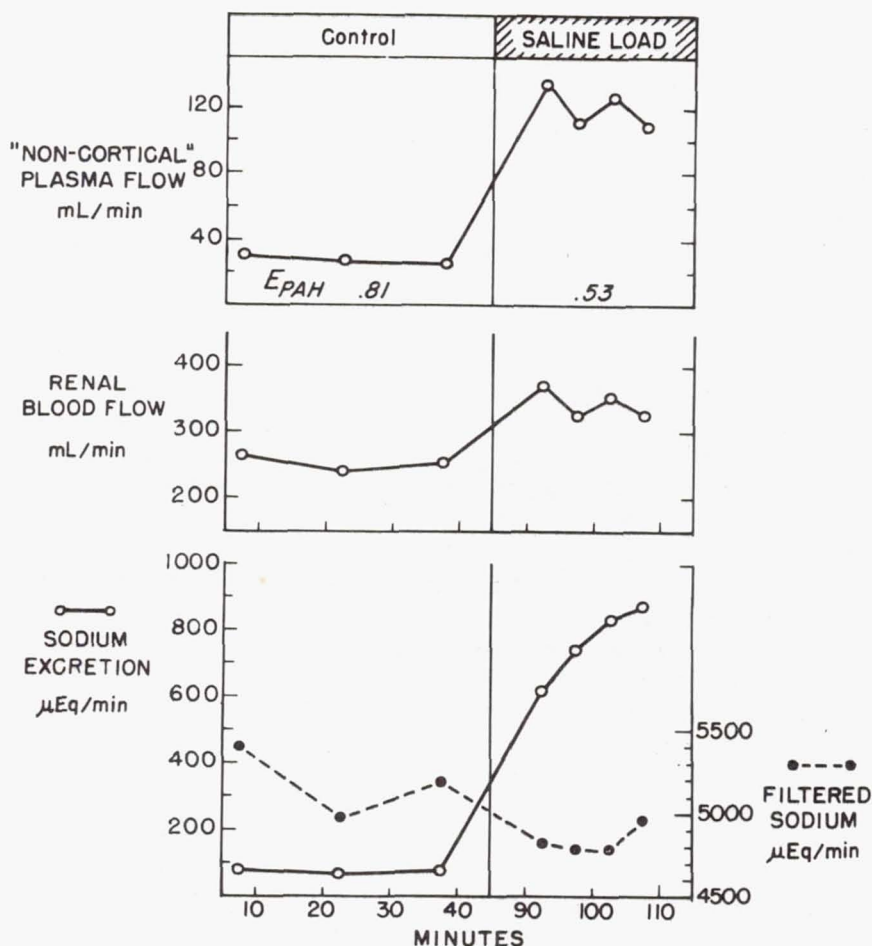
Figure 1.- Graph of "non-cortical" plasma flow,
renal blood flow, and sodium excretion.

sodium excretion usually decreased somewhat in the control kidneys.
When arterial pressure was increased an average of 33 mm Hg by the
infusion of angiotensin (shown in the third column) a further increase
in sodium excretion occurred in the vasodilated kidneys. This addi-
tional increased excretion of sodium was independent of changes in
glomerular filtration, and occurred despite decreases in renal plasma
flow produced by the vasoconstrictor effect of the antiotensin. In
the control kidneys, sodium excretion during the pressor infusion re-
mained depressed in all but three experiments.

Similar observations have been made when arterial pressure was in-
creased by norepinephrine, and sub-pressor infusions of angiotensin have
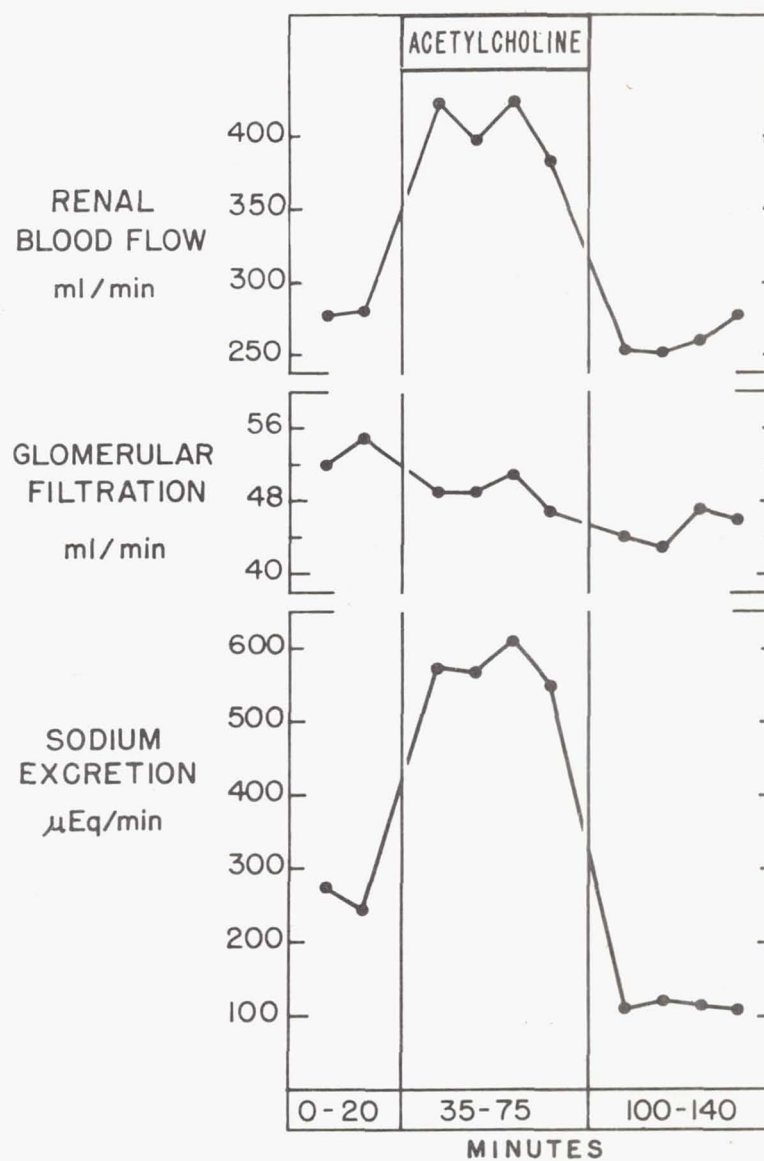
Figure 2.- Representative study of unilateral renal vasodilatation
by the infusion of acetylcholine into one renal artery.
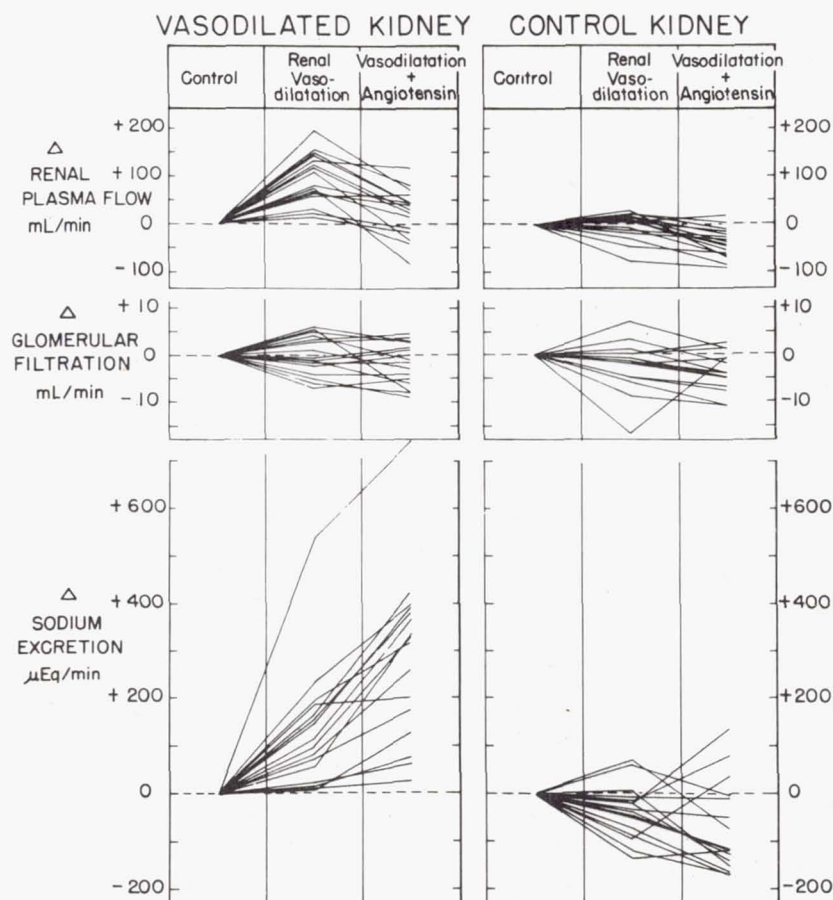
Figure 3.- Graphic illustrations of the effects of combined
renal vasodilatation and increased arterial pressure.

not produced increased excretion of sodium. A comparison of the pressor
effects of angiotensin and norepinephrine is shown on figure 4. Vasodi-
latation produced by acetylcholine resulted in a three-fold increase in
renal blood flow and a moderate increase in sodium excretion. When
angiotensin was infused intravenously to increase arterial pressure
60 mm Hg, the excretion of sodium increased further without an increase
in glomerular filtration. Blood pressure and sodium excretion were
allowed to decrease, and then the same elevation in pressure was pro-
duced by infusing norepinephrine. This resulted in a similar increase
in sodium excretion without increased glomerular filtration or blood
flow. Again, the same effects could be achieved after discontinuing
norepinephrine and re-infusing angiotensin. We believe that these are
effects of renal perfusion pressure, and not direct renal effects of
the drugs.
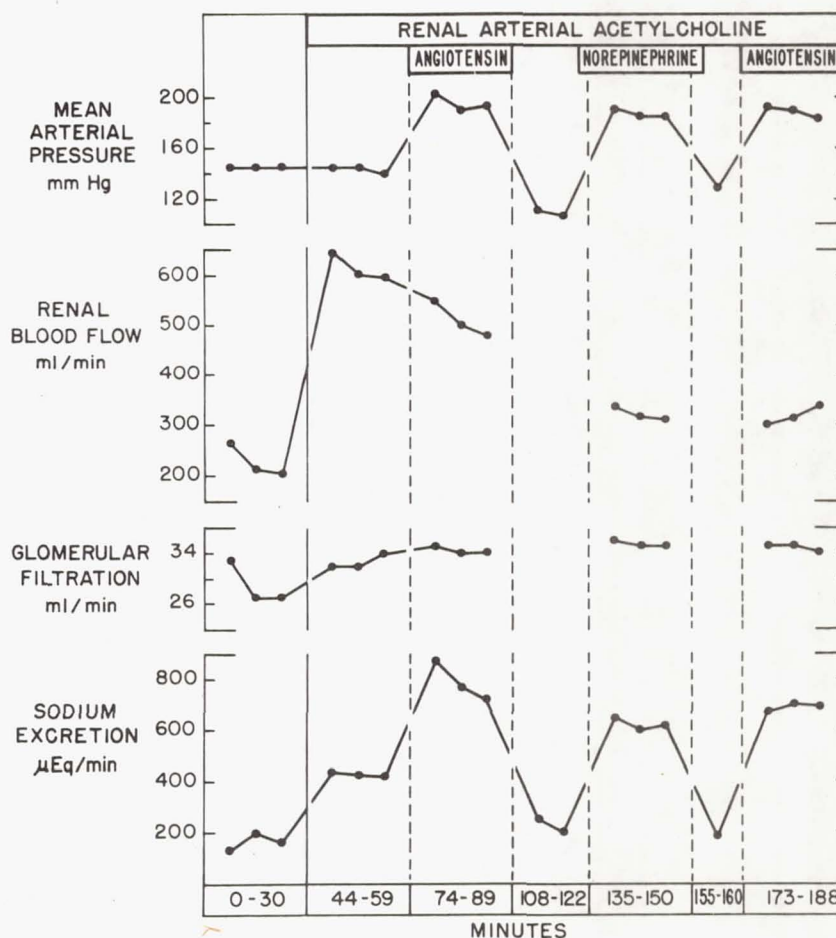
Figure 4.- Comparison of the pressor effects of
angiotensin and norepinephrine.

These studies are consistent with the view that renal vascular resistance and perfusion pressure may play important roles in determining tubular reabsorption and the rate of sodium excretion. These hemodynamic factors could therefore be physiologic variables involved in regulating the volume of the extracellular fluid compartment.

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A COMPARATIVE STUDY OF THE PHYSIOLOGICAL EFFECTS OF

IMMERSION AND RECUMBENCY

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Attempting to study the physiological manifestations of space flight on earth is frustrating and, at best, an approximation of reality. There is nothing wrong with an approximation provided it gives useful information. The history of science is studded with approximations!

The approximations useful in the study of deconditioning of man in space are bed rest and fluid immersion. We would like to compare these approximations because we would like to compare the data obtained using the two different methods with each other and with observations made during space flight. Further, because extremely rapid physiological changes have been reported during fluid immersion, we thought it might be possible to perform "weightless" studies in a much shorter period by the use of immersion techniques. This would allow more economical and frequent studies with larger numbers of subjects. While we were in this nascent phase, we were informed by NASA of work done by Dr. Gerou. Dr. Gerou is a plastic surgeon at Baylor University who had been using an immersion technique to treat severely burned patients. He immersed the patients in silicone oil until they reached the stage of healing which would allow a skin graft. He reported normal skin showed no ill effects after being continuously immersed in silicone oil for periods up to 30 days. Taking a page from Dr. Gerou, we designed a study for subjects to be immersed to neck level in silicone oil and in a position similar to bed rest. (See fig. 1.)

These tanks had temperature controls, oil filters, and pump. They were completely independent of each other so no cross contamination could occur.

Each subject was immersed to neck level 24 hours per day for 10 days. The only time allowed out of the oil was for testing or emunctory functions.

During each study there were three subjects immersed in silicone oil. Simultaneously three subjects were at absolute bed rest. After the study ended, the bed-rest and oil-immersion subjects were ambulated

DOUGLAS IMMERSION STUDIES
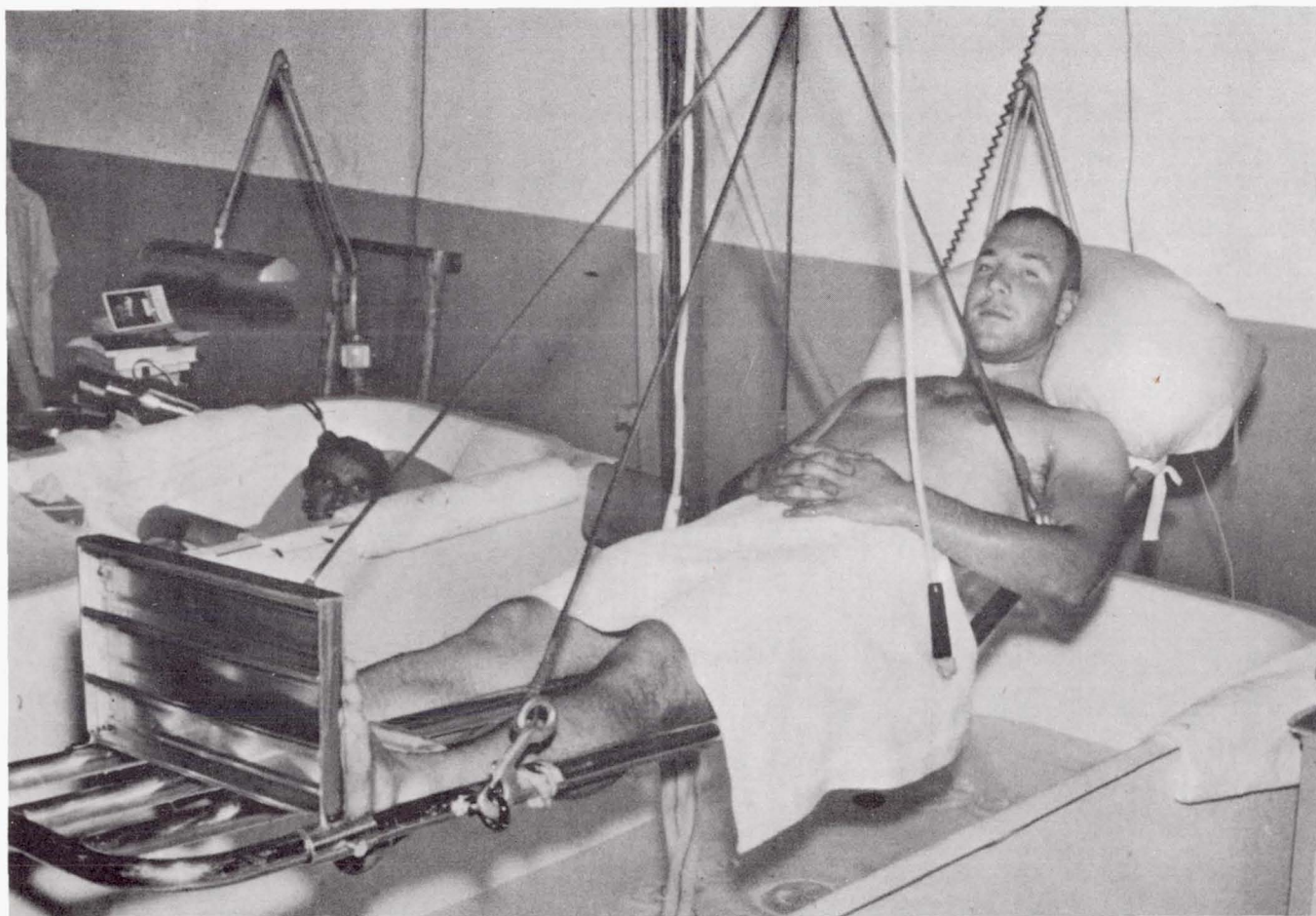
Figure 1

for 6 weeks, reconditioned physically so that their MOI's were comparable to the initial state, and returned to bed rest and oil immersion. The second study reversed the subjects so that those who were previously at bed rest were immersed in oil and those who were previously in oil were at bed rest. In this way, there were double controls because each subject was compared to himself in each environment and to a subject who was simultaneously in a different environment.

Functional and biochemical tests were performed on each man and table I in the appendix is the tabulation of these tests.

A few key studies will be presented. Other studies and summary tables are contained in the appendix of this article.

A summary table showing the frequency of syncope is shown on page 129 in the appendix. The presence or absence of deconditioning is not judged by whether or not syncope occurs, but it does serve as a rough guide of its severity.

The table on page 136 in the appendix shows the differences between bed rest and oil immersion subjects with regard to plasma and blood volume and fluid compartment changes.

The table on page 143 in the appendix shows the oxygen consumption of of subjects at rest in both environments.

Finally, the table on page 141 in the appendix shows a comparison of the MOI obtained by each subject upon ambulation after bed rest and oil immersion.

As a general conclusion, oil immersion and bed rest cause similar kinds of deconditioning provided great care is taken with temperature control and negative pressure breathing. We have evidence that oil immersion causes a greater degree of physiological deconditioning than bed rest, but we did not see the much greater magnitude of "deconditioning" that has been reported with fluid immersion.

I will briefly discuss the short radius centrifuge study that we have completed (see fig. 5). This study was designed to determine whether the short radius centrifuge could prevent the cardiovascular deconditioning observed during bed rest and whether it could be used as a test device, that is, similar to the tilt table to determine the presence of cardiovascular deconditioning. A radius of 37 inches from the axis of rotation to heart level and 72 inches from the axis of rotation to the feet was chosen. This radius provided a 100 percent gradient between the heart and the feet.
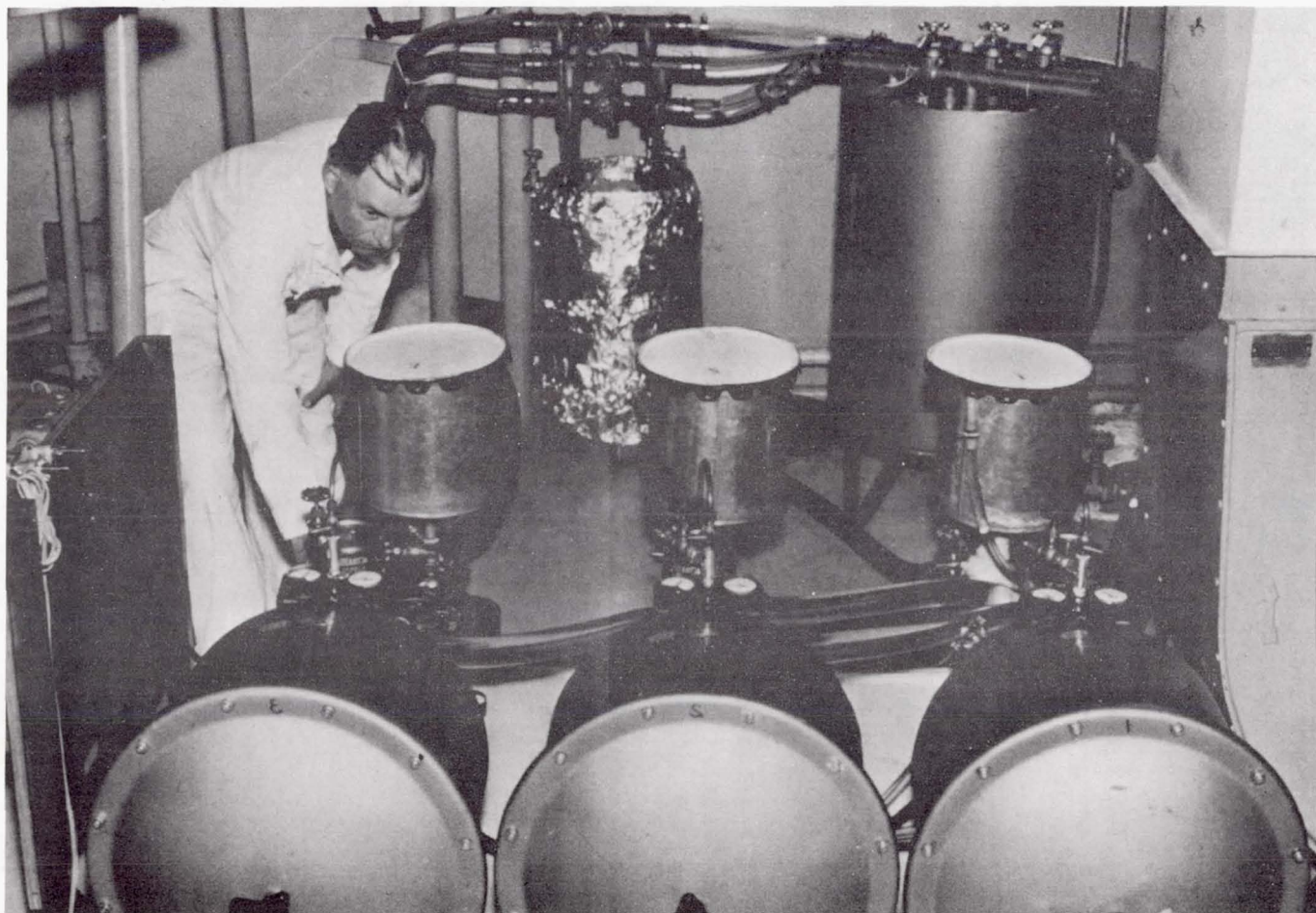
DOUGLAS IMMERSION STUDIES

Figure 2

DOUGLAS IMMERSION STUDIES
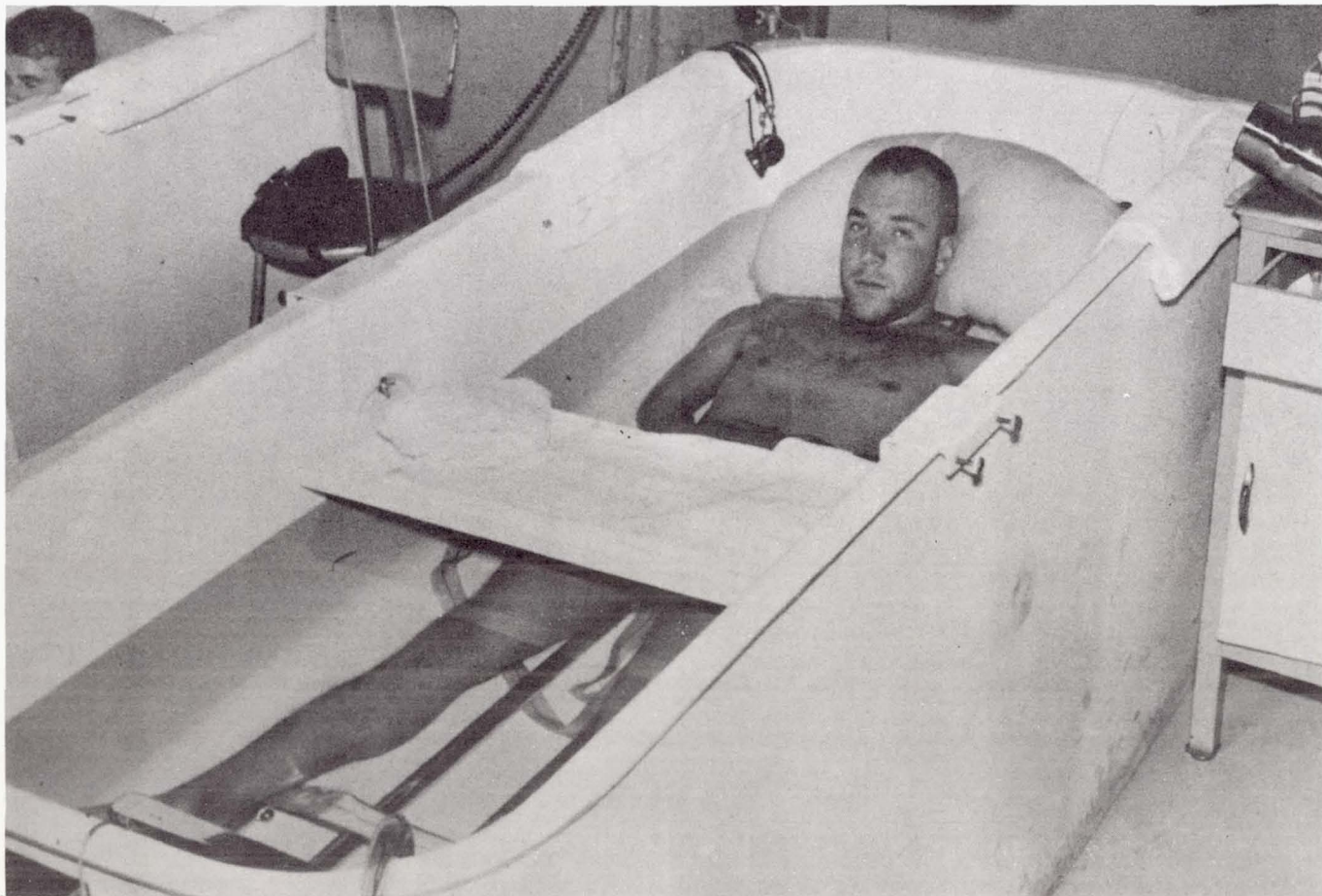
Figure 3

DOUGLAS IMMERSION STUDIES
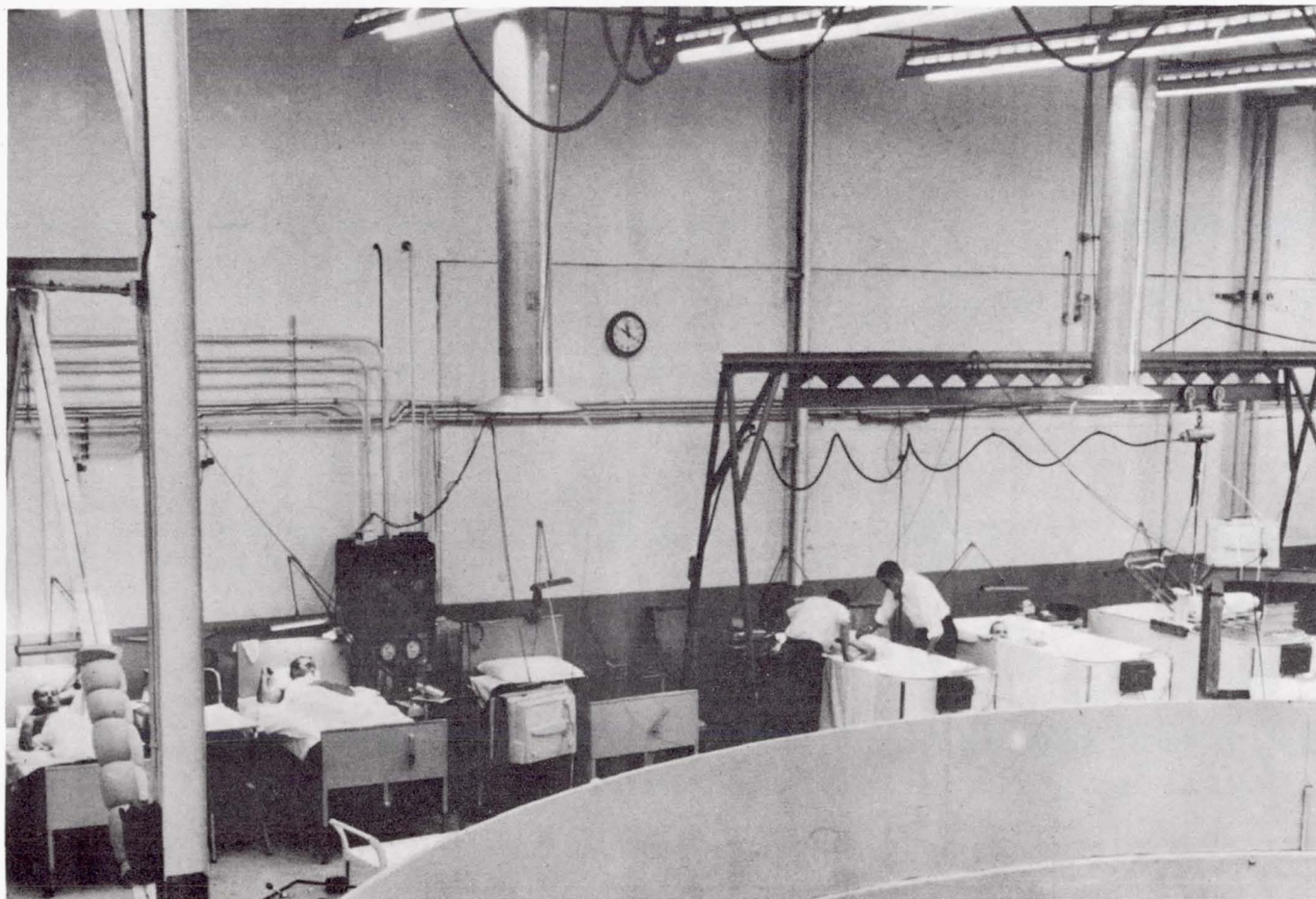
Figure 4
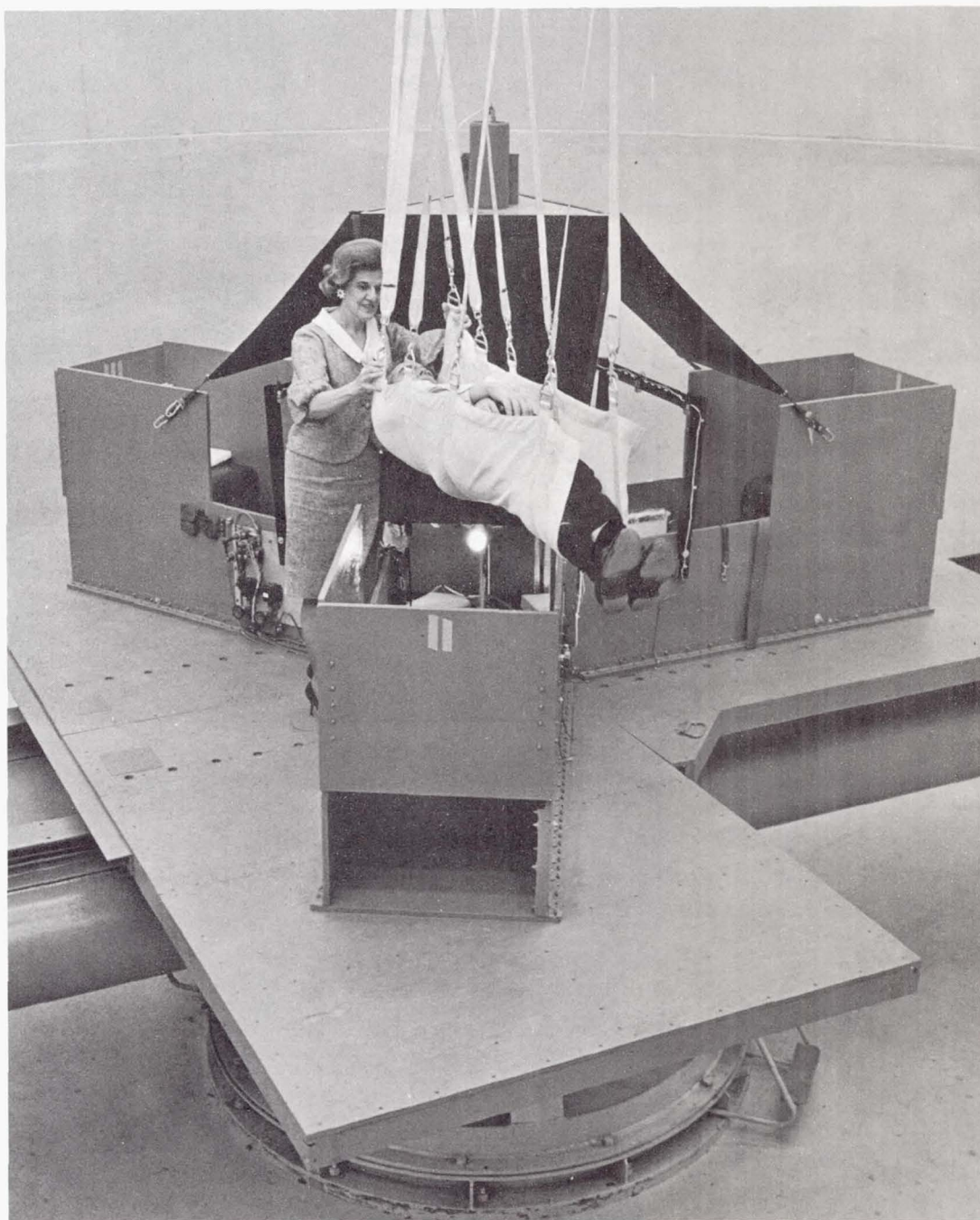
Figure 5

Eight subjects were placed at absolute bed rest, six subjects rode the centrifuge for a 20-minute period four times a day for a total of 80 minutes per day per subject. They were ridden at +3.5 - 4 g_z at the feet and two other subject had a step function bioassay ride every other day.

The section of the appendix containing the tilt table studies graphically illustrates the tilts for each subject before the study began and after it was concluded but before the subjects were ambulated. Taken individual by individual, it can be seen that with one exception, which I think was an error, all subjects riding the centrifuge four times per day maintained a good tilt table tolerance. Obviously, cardiovascular deconditioning was not 100 percent prevented as indicated by higher heart rates and slightly narrower pulse pressures than before the study. However, those acquainted with such studies will agree they are much better than those seen after straight bed rest.

One of the most striking findings measured during this study was the change in acceleration tolerance seen in deconditioned subjects and its return towards normal with ambulation. This is shown on the page titled Bioassay Step Functions and all the values are g_z at heart level.

Finally we were able to show with step function bioassay runs and endurance studies that the short radius centrifuge is an excellent tool with which to measure the amount of cardiovascular deconditioning present.

In conclusion, I wish to emphasize four points and these are:

1. Silicone oil immersion and bed rest cause similar types of deconditioning with a slight edge for oil immersion.

2. The SRC can largely prevent cardiovascular deconditioning seen at bed rest.

3. The SRC is an excellent tool to measure the presence of cardiovascular deconditioning.

4. There is a severe loss of g tolerance in subjects deconditioned at bed rest.

APPENDIX

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TABLE I

BASELINE AND INTERCURRENT MEASURES

TESTS	DATE OF DETERMINATION			
FUNCTIONAL				
Passive tilt test	B-1	T-2, T-4, T-8		BR-1
Negative pressure boot	B-2	T-5		BR-2
Treadmill MOI test	B-3			BR-3
Ergometer MOI test	B-2			BR-2
Master's two-step	B-1			BR-3
Respiratory function	B-1	T-5		BR-1
Posture test	B-3			BR-2
Acceleration tolerance test	B-2			BR-2
Audiometry	B-1			BR-3
Body weight and composition	B-3			BR-3
Bone density	B-1			BR-3
Chest film	B-1			BR-3
BIOCHEMICAL				
Total body water $(H_2{}^3O)_{82}$	B-1	T-5, T-10		-
Extracellular fluid (Br^{82})	B-1	T-5, T-10		-
Plasma and blood volumes (T-1824)	B-3	T-5, T-10		-
Urine - electrolytes, Ca, P, creatinine, osmolarity, specific gravity, routine, micro, pH	B-3	T-2, 4, 6, 8, 10-		
17-OH*, 17 ketos*, phosphate*, aldosterone*, catecholamines*	TBD			
Blood - electrolytes, Ca, P, electrophoresis, protein, creatinine, hematocrit, hemoglobin, RBC count, and morphology, platelets count and morphology, WBC count, morphology and differential	B-1	T-5, T-10		-
17-hydroxycorticosteroids*, aldosterone*	TBD			
Water balance	Continuous			
Sample diet	T-2			
MONITORING				
Blood pressure				
Heart and respiration rates				
Temperature				
Fluid intake/output				
Physical examination	Daily			
Oil inspection				
Body weight				
ECG & phonocardiogram				

Baseline (B)
Experiments (T)
Baseline-Recovery (BR)

*Analyzed by NASA-MSC

PHYSICAL CHARACTERISTICS

OF SUBJECTS

SUBJECT	AGE	HEIGHT (cm)	WEIGHT (Kg)	PLASMA VOLUME/ LEAN MASS (ML/Kg)
BB	22	177.2	75.15	57.0
LB	26	168.9	61.11	42.7
EH	22	181.4	68.53	61.1
JH	21	174.6	71.98	63.1
BI	22	185.7	75.42	60.0
GK	22	176.6	88.73	57.9
LL	22	176.9	78.77	56.6
RM	25	190.5	83.49	53.6
BS	22	177.5	74.16	52.8
LS	24	174.6	71.20	58.4
WW	26	180.6	74.43	56.0

INCIDENCE OF SYNCOPE

DURING TILT

DATE OF DETERMINATION	Silicone Immersion			Bed Rest		
	Number of Subjects	Subjects Developing Syncope	Percent Syncope	Number of Subjects	Subjects Developing Syncope	Percent Syncope
T-2	11	6	54%	11	4	36%
T-4	10	5	50%	10	4	40%
T-8	10	7	70%	10	3	30%
T-10	9	4	44%	10	4	40%

HEART RATE, PULSE PRESSURE
AND MEAN ARTERIAL PRESSURE
DURING TILT

SUBJECT	PARAMETER	DATE OF DETERMINATION									
		B-3		T-2		T-4		T-8		T-10	
		Sili-cone	Bed Rest	Sili-cone	Bed Rest	Sili-cone	Bed Rest	Sili-cone	Bed Rest	Sili-cone	Bed Rest
BB	HR	95	93	117	115	131	122	126	121	132	120
	PP	29	26	13	34	12	18	16	23	16	24
	MAP	98	100	97	99	97	97	94	101	89	95
LB	HR	87	68	93	72	102	83	109	80	99	75
	PP	28	30	21	34	21	45	35	40	35	43
	MAP	95	95	104	90	89	87	95	90	93	90
EH	HR	75	67	78	77	80	83	81	82	96	95
	PP	28	25	17	18	20	21	29	24	21	23
	MAP	97	96	97	92	98	93	95	91	101	92
JH	HR	80	82	128	119	128	132	120	127	133	129
	PP	35	42	12	25	9	12	13	25	10	12
	MAP	98	107	100	98	92	103	95	103	92	101
BI	HR	75	74	114	99	124	110	130	108	111	98
	PP	26	26	13	28	15	29	10	16	19	24
	MAP	93	95	93	94	94	90	92	96	85	90
GK	HR	72	72	88	79	●	●	●	●	●	●
	PP	26	26	13	18	●	●	●	●	●	●
	MAP	99	99	96	96	●	●	●	●	●	●
LL	HR	116	83	140	120	148	125	139	138	148	134
	PP	50	33	26	30	32	27	39	39	25	29
	MAP	109	102	103	98	98	97	98	106	96	105
RM	HR	69	76	91	83	100	94	87	87	●	86
	PP	27	25	20	27	11	15	19	20	●	19
	MAP	102	100	99	98	100	100	96	96	●	98
BS	HR	74	67	110	90	111	86	97	97	111	98
	PP	26	25	18	14	15	27	21	17	19	17
	MAP	100	97	95	92	99	94	96	87	97	95
LS	HR	72	72	76	74	93	83	80	72	77	82
	PP	30	30	19	22	18	23	17	32	19	25
	MAP	98	95	90	89	92	90	93	87	90	87
WW	HR	61	67	82	103	114	103	104	115	110	112
	PP	35	32	16	16	21	18	23	11	12	19
	MAP	94	95	94	97	99	100	102	96	100	98
MEAN	HR	79.6	74.6	101.5	93.7	113.1	102.1	107.3	102.7	113.0	102.9
	PP	30.9	29.0	17.0	24.1	17.4	23.5	22.2	24.7	19.5	23.5
	MAP	98.4	98.2	97.0	94.8	95.8	95.1	95.6	95.3	93.6	95.7

o = Subject withdrawn from program

ORTHOSTATIC TOLERANCE SUMMARY

SUBJECT	DATA OF DETERMINATION									
	B-3		T-2		T-4		T-8		T-10	
	Silicone	Bed Rest	Silicone	Bed Rest	Silicone	Bed Rest	Silicone	Bed Rest	Silicone	Bed Rest
BB	O	O	O	O	O	O	+	O	+	O
LB	O	O	O	O	+	O	O	O	O	O
EH	O	O	O	O	O	O	+	O	O	O
JH	O	O	+	O	+	+	+	O	+	+
BI	O	O	+	O	O	+	+	+	+	+
GK	O	O	+	+	●	●	●	●	●	●
LL	O	O	O	O	O	+	O	O	O	+
RM	O	O	O	O	O	O	O	O	●	O
BS	O	O	+	+	+	O	+	+	O	O
LS	O	O	+	+	+	+	+	+	+	+
WW	O	O	+	+	+	O	+	O	O	O

O = No Syncope

+ = Syncope

● = Subject withdrawn from program

ACCELERATION TOLERANCE

| SUBJECT | DATE OF DETERMINATION | | | |
| | Baseline | | Baseline - Recovery | |
	Silicone	Bed Rest	Silicone	Bed Rest
BB	4.5	4.8	4.6	4.2
LB	5.0*	5.0*	4.7	4.8
EH	3.7	5.0*	2.8	3.9
JH	4.0	4.0	3.5	3.6
BI	2.5	3.8	2.9	3.2
GK	3.9	●	●	●
LL	3.8	3.4	1.5[†]	3.5
RM	4.3	3.1	●	3.8
BS	3.0	3.4	3.3	2.3
LS	3.2	2.8	3.6	3.2
WW	4.8	4.0	4.2	4.3
Mean	3.77	3.66	3.7	3.68

All Entries in $+G_z$ units at heart level

* Terminated at maximum G; not included in mean

† Terminated because of marked tachycardia; not included in mean

● Subject withdrawn from program

POSTURE TESTS

SUBJECT	MEDIUM	DATE OF DETERMINATION					
		Baseline			Baseline - Recovery		
		Walk *	Stand-Eyes Open **	Stand-Eyes Closed **	Walk	Stand-Eyes Open	Stand-Eyes Closed
L. L.	Silicone	14	31	146	11	24	30
	Bed	13	22	13	11	18	29
J. H.	Silicone	15	52	24	11	16	19
	Bed	10	21	15	5	12	18
B. S.	Silicone	15	180	180	13	16	139
	Bed	15	84	180	15	43	180
W. W.	Silicone	14	28	40	13	19	17
	Bed	15	24	61	11	21	70
G. K.	Silicone	14	14	54	--	---	---
	Bed	11	18	49	13	44	73
E. H.	Silicone	14	18	20	15	24	16
	Bed	15	151	88	13	67	24
L. S.	Silicone	15	180	180	15	180	165
	Bed	15	152	180	15	100	150
L. B.	Silicone	15	45	87	15	66	69
	Bed	15	30	79	15	101	158
B. I.	Silicone	15	56	42	14	20	42
	Bed	8	47	49	14	23	36
R. M.	Silicone	15	52	37	12	33	28
	Bed	13	61	80	10	22	32
B. B.	Silicone	14	28	108	10	13	41
	Bed	8	31	102	14	14	75

* = steps
** = sec

133

134

POSTURE TESTS

CHANGES IN ABILITIES

	WALKING			
	Silicone Immersion		Bed Rest	
	Baseline	Baseline - Recovery	Baseline	Baseline - Recovery
Total Steps	160	129	138	136
Change	-31		-2	
Average of Total	14.5	12.9	12.5	12.3
Change	-1.6		-0.2	
Decrease in Ability	-19%		-1.5%	
	STANDING - EYES CLOSED			
Total Seconds	918	566	896	845
Change	-352		-51	
Average of Total	83.4	56.6	81.4	76.8
Change	-26.8		-4.6	
Decrease in Ability	-32%		-6%	
	STANDING - EYES OPEN			
Total Seconds	684	411	641	465
Change	-273		-176	
Average of Total	62.1	41.1	58.2	42.2
Change	-21		-16	
Decrease in Ability	-34%		-27%	

BODY WEIGHT AND COMPOSITION

| SUBJECT | MEDIUM | DATE OF DETERMINATION | | | | | |
| | | Baseline | | | Baseline - Recovery | | |
		Total	Lean	Fat	Total	Lean	Fat
BB	Silicone	76.84	59.20	17.60	74.27	56.0	18.3
	Bed Rest	75.15	57.30	17.85	74.12	54.56	19.56
LB	Silicone	61.11	47.45	13.66	60.32	45.92	14.4
	Bed Rest	60.44	50.00	10.40	59.3	50.2	9.1
EH	Silicone	68.53	58.26	10.27	68.32	57.66	10.66
	Bed Rest	68.09	59.50	8.60	66.52	60.00	6.50
JH	Silicone	72.25	52.8	19.5	70.01	50.2	19.8
	Bed Rest	71.98	50.5	21.5	70.67	50.1	20.6
BI	Silicone	75.09	63.0	12.1	71.80	62.8	9.0
	Bed Rest	75.42	57.72	17.7	72.45	60.15	12.3
GK	Silicone	88.73	62.5	26.2	87.37	●	●
	Bed Rest	●	●	●	●	●	●
LL	Silicone	78.38	63.6	14.7	76.5	63.3	13.2
	Bed Rest	78.77	58.7	20.1	77.59	61.0	16.6
RM	Silicone	83.52	72.9	14.6	82.12	74.9	7.2
	Bed Rest	83.49	●	●	81.49	71.44	10.05
BS	Silicone	74.16	60.7	13.5	73.7	61.3	12.4
	Bed Rest	74.22	63.8	10.4	73.73	62.9	10.9
LS	Silicone	71.2	61.32	9.88	69.91	59.57	10.34
	Bed Rest	71.41	61.6	9.8	69.99	61.8	8.2
WW	Silicone	74.43	62.1	12.3	72.39	60.9	11.5
	Bed Rest	75.19	64.9	10.3	72.91	64.0	8.9

Entries are in Kg
● Subject Withdrawn from program

AVERAGE FLUID COMPARTMENT VALUES

COMPARTMENT	MEDIUM	B-1	T-5			T-10		
		VOLUME	VOLUME	PERCENT CHANGE	CHANGE	VOLUME	PERCENT CHANGE	CHANGE
Plasma Volume	Silicone	3238	2509	-23%	-729	2804	-13%	-434
	Bed Rest	3285	2816	-14%	-469	2796	-15%	-489
Total Blood Volume	Silicone	5497	4780	-13%	-717	4970	-10%	-527
	Bed Rest	5543	5123	- 8%	-420	4919	-11%	-624
Red Cell Volume	Silicone	2257	2271	+ 1%	+14	2165	- 4%	- 92
	Bed Rest	2256	2307	+ 2%	+51	2121	- 6%	-135
Total Body Water	Silicone	46.68	44.60	- 4%	-2.08	47.57	+ 2%	+0.89
	Bed Rest	46.86	47.40	+ 1%	+0.54	47.81	+ 2%	+0.95
Extra Cellular Water	Silicone	18.69	18.05	- 3%	-0.64	17.71	- 5%	-0.98
	Bed Rest	18.73	18.32	- 2%	-0.41	17.44	- 7%	-1.29

Plasma Volume, Total Blood Volume and
Red Cell Volume in ML

Total Body Water and
Extra Cellular Water in L

FLUID COMPARTMENTS

SUBJECT	MEDIUM	METHOD OF DETERMINATION														
		B-1					T-5					T-10				
		Plasma Volume	Total Blood Volume	Red Cell Volume	Total Body Water	Extra-Cellular Water	Plasma Volume	Total Blood Volume	Red Cell Volume	Total Body Water	Extra-Cellular Water	Plasma Volume	Total Blood Volume	Red Cell Volume	Total Body Water	Extra Cellular Water
BB	Silicone	3160	5550	2390	44.7	18.3	2320	45??	2240	----	17.6	2675	5050	2370	44.0	17.6
	Bed Rest	3265	5560	2290	45.2	18.9	30?0	53??	2730	48.8	17.9	2615	4650	2060	54.2	18.9
LB	Silicone	2025	3450	1420	36.7	14.2	1730	32??	1530	35.8	14.3	1810	3040	1230	38.8	14.2
	Bed Rest	2230	3670	1440	36.3	14.5	1730	31?	1350	----	13.6	1760	3050	1290	32.8	13.5
EH	Silicone	3555	6050	2490	47.0	18.5	2960	504?	3030	46.0	18.8	2840	5000	2160	56.3	16.5
	Bed Rest	3630	5960	2280	49.6	19.3	2550	4500	1950	----	18.7	2745	4750	2000	45.3	18.9
JH	Silicone	3395	5600	2200	40.5	17.2	2425	44??	1990	33.7	17.0	2630	4630	2000	39.7	16.9
	Bed Rest	3185	5250	2060	40.8	18.0	2585	472?	2130	41.8	17.5	2760	4700	1940	36.0	17.2
BI	Silicone	3220	5490	2270	48.5	21.0	2520	47??	2260	----	18.3	2705	4930	2220	44.3	18.6
	Bed Rest	3460	5800	2340	48.3	20.9	3580	652?	2940	47.0	18.9	2765	4860	2090	45.0	19.1
LL	Silicone	3140	5440	2300	45.7	18.1	2535	47??	2170	48.2	18.9	2865	5130	2260	43.1	18.4
	Bed Rest	3325	5860	2530	49.6	19.1	2560	492?	2360	47.4	19.0	2995	5370	2370	51.2	18.6
RM	Silicone	3620	6060	2440	57.9	21.9	2960	530?	2340	----	20.5	4020	6520	2500	55.3	22.0
	Bed Rest	4020	6630	2610	60.1	21.9	3630	65??	2870	55.5	21.3	3370	6030	2660	5?.0	11.3
BS	Silicone	3205	5200	1990	45.0	19.0	2290	425?	1960	51.8	18.2	2760	4860	2100	50.0	17.9
	Bed Rest	2935	5160	2220	45.9	17.3	2700	47??	2060	45.0	19.2	2820	4890	2070	56.3	16.6
LS	Silicone	3580	6200	2620	47.0	19.1	2805	550?	2700	47.0	18.6	2750	5200	2450	45.2	16.9
	Bed Rest	2860	5120	2260	48.0	18.4	2730	490?	2260	----	17.9	2755	5030	2290	52.5	19.2
WW	Silicone	3480	5930	2450	53.8	19.6	2540	49??	2440	43.7	18.3	2960	5340	2360	56.0	18.1
	Bed Rest	3385	6420	2530	44.8	19.0	3010	54??	2390	46.3	15.8	3340	5750	2440	46.3	17.6

Plasma Volume, Total Blood Volume and
Red Cell Volume in ML

'Total Body Water and
Extra Cellular Water in L

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BLOOD CHEMISTRIES

TEST	MEDIUM	BB				LB				EH				JH				BI				GK				LL				RM				BS				LS				WW			
		B	T-5	T-10	BR	B	T-5	T-10	BR	B	T-5	T-10	BR	B	T-5	T-10	BR	B	T-5	T-10	BR	B	T-5	T-10	BR	B	T-5	T-10	BR	B	T-5	T-10	BR	B	T-5	T-10	BR	B	T-5	T-10	BR	B	T-5	T-10	BR
Hbg	Silicone	14.7	16.1	15.7		15.1	16.5	14.2		14.3	16.2	15.2		13.9	16.3	15.4		14.2	15.9	16.1		15.7	16.5	•		15.2	15.9	16.6		15.8	15.5	13.7		13.3	15.7	15.4		14.6	16.9	16.6		14.2	16.0	15.4	
	Bed Rest	14.6	16.3	15.5		13.4	15.5	15.7		13.8	14.7	15.5		13.9	15.7	15.0		14.3	15.3	14.6		15.7	•	•		15.0	17.2	17.5		14.6	15.9	15.1		15.2	15.1	16.1		16.1	16.8	16.2		13.7	15.0	14.3	
Hct	Silicone	45	51	49		43	49	42		43	49	45		41	47	45		43	49	47		47	51	•		44	45	46		42	46	40		40	48	45		44	51	49		43	51	46	
	Bed Rest	43	49	46		41	46	44		40	45	44		41	47	43		42	47	46		•	51	•		45	45	46		41	46	46		45	45	44		46	47	47		46	47	44	
RBC	Silicone	4.3	5.1	5.6		5.3	5.8	5.1		5.3	5.7	5.5		4.7	4.8	5.1		4.6	5.1	5.4		•	5.8	•		5.4	5.1	4.8		4.5	5.4	4.9		•	5.5	4.7		5.2	5.9	5.7		•	5.6	5.1	
	Bed Rest	5.2	5.8	5.4		4.5	5.4	5.4		4.8	5.3	5.5		•	5.6	5.4		5.2	5.4	5.2		5.1	•	•		•	5.0	5.0		5.4	5.5	5.0		5.1	5.0	5.1		4.9	5.3	5.5		5.3	4.6	5.4	
WBC	Silicone	9,400	7,200	7,800		8,200	9,100	6,600		8,000	6,900	7,300		5,500	7,200	7,200		6,800	7,300	7,600		5,500	7,500	•		7,800	6,600	7,200		3,400	7,000	5,500		4,400	5,400	7,600		5,700	8,300	7,400		4,500	5,900	7,710	
	Bed Rest	9,600	8,000	8,000		4,500	6,000	5,700		6,100	4,900	5,600		6,200	4,900	6,700		8,900	6,300	9,300		6,600	•	•		6,000	6,600	6,300		7,000	8,300	8,100		4,000	•	6,900		6,000	5,200	6,100		4,900	6,100	6,200	
Na+	Silicone	141	140	143		144	141	146		144	143	143		144	144	137		138	137	138		138	142	•		134	135	138		140	136	137		140	142	138		144	147	145		141	147	144	
	Bed Rest	146	143	152		145	139	132		140	137	136		145	145	149		145	144	146		137	•	•		140	141	143		141	142	154		135	138	133		141	140	138		141	140	133	
K+	Silicone	4.7	4.4	4.9		4.3	5.7	4.5		5.1	5.3	5.0		4.8	5.2	5.3		4.3	4.3	4.2		5.1	5.0	•		4.7	4.9	4.6		4.6	4.0	4.6		4.4	4.5	4.4		4.4	5.5	4.7		5.2	5.1	5.5	
	Bed Rest	5.1	5.0	5.4		4.2	3.8	4.2		4.3	4.1	4.4		5.0	5.3	5.8		4.8	4.8	4.6		5.2	•	•		4.8	5.0	4.9		4.6	4.9	4.6		4.9	5.1	4.3		4.1	4.0	4.2		5.3	5.4	4.7	
CL-	Silicone	106	99	101		100	105	98		103	103	100		104	91	111		104	100	103		105	100	•		109	90	104		102	100	101		108	103	105		103	104	105		106	104	105	
	Bed Rest	101	109	107		108	98	100		104	103	102		106	106	107		103	108	105		102	•	•		108	104	99		103	107	100		104	93	109		108	102	99		104	92	106	
HCO3-	Silicone	26	22	26		35	27	36		29	25	37		29	34	25		25	25	26		28	34	•		29	33	28		27	24	28		27	35	25		32	24	35		28	33	24	
	Bed Rest	34	25	31		28	24	27		23	23	27		24	35	23		32	27	34		30	•	•		30	32	25		35	22	36		29	34	26		23	22	22		29	32	28	
Ca++	Silicone	4.9	5.2	5.1		4.8	5.1	5.1		4.6	5.2	5.2		5.2	5.7	5.3		5.0	5.9	5.2		4.8	5.0	•		4.9	5.1	5.0		5.0	5.0	4.8		4.8	5.0	4.8		4.2	4.7	4.7		4.7	5.3	4.9	
	Bed Rest	4.5	4.9	5.2		5.0	5.5	5.2		4.9	5.2	5.1		5.0	5.5	5.3		4.7	5.1	5.0		5.2	•	•		4.7	5.1	4.8		4.7	5.1	4.6		5.2	5.2	4.9		5.1	5.7	5.2		5.1	4.8	4.7	
P	Silicone	3.0	3.5	4.3		3.8	3.6	3.8		4.6	4.3	4.0		3.2	3.2	3.8		2.8	2.5	3.8		2.2	3.4	•		3.2	3.1	4.1		3.1	3.0	3.9		3.1	3.4	3.1		3.8	3.4	2.6		3.3	4.0	3.5	
	Bed Rest	4.6	3.6	3.4		2.6	2.9	3.6		4.9	3.8	4.4		3.1	3.5	2.5		3.7	3.9	2.5		3.1	•	•		3.1	3.4	3.0		3.6	3.9	3.7		3.0	4.1	3.1		2.9	3.2	3.3		3.3	3.6	3.8	
Cephalin Flocculation	Silicone	0	0	0		0	0	0		3+	2+	0		•	2+	0		0	0	1+		0	•	•		•	2+	0		2+	0	2+		1+	2+	0		0	0	2+		1+	1+	0	
	Bed Rest	0	0	1+		0	0	0		3+	1+	3+		1+	3+	2+		2+	2+	2+		1+	•	•		2+	2+	0		2+	3+	2+		1+	1+	3+		0	1+	0		1+	1+	0	
Creatinine	Silicone	1.12	1.20	0.96		1.20	0.94	1.00		1.20	0.98	1.00		0.94	1.10	0.96		1.05	1.00	0.93		0.89	1.20	•		0.97	1.30	1.00		1.13	0.97	0.77		1.00	1.20	1.60		0.99	1.10	1.00		0.98	0.85	1.40	
	Bed Rest	1.10	1.00	1.60		1.11	0.89	0.84		1.07	0.98	0.82		1.20	0.94	1.40		1.20	1.20	1.00		1.10	•	•		1.00	0.54	1.30		0.98	0.93	1.20		1.30	1.20	1.10		0.92	1.20	0.96		1.06	0.95	0.85	
Thymol Turbidity	Silicone	2	1	1		9	6	5		4	3	5		3	4	5		5	6	5		5	5	•		•	3.5	5		5	4	2		3	6	4		3	3	4		3	3	2	
	Bed Rest	1	1	1		6	8	4		3	6	5		3	5	5		9	7	7		5	•	•		2	4	3		5	4	2		3	6	4		0	3	4		0	1	2	
SGOT	Silicone	38	23	25		42	25	35		23	29	18		39	23	25		28	28	28		39	26	•		27	23	23		26	23	23		40	33	13		30	29	25		29	28	30	
	Bed Rest	26	22	24		31	27	26		20	22	23		55	30	23		39	31	33		•	•	•		20	22	22		30	22	29		30	22	29		26	23	30		26	23	30	
BSP (Retention)	Silicone	0.1			2.0	5.3			2.7	2.5			3.0	3.6			2.3	2.0			•	4.6			3.4	0.1			1.4	1.3			2.4	0.2			2.5	1.6			3.0	1.8			1.6
	Bed Rest	2.5			1.0	•				•				•				2.7			3.0	•				•				2.8			2.0	•				•				•			

Hbg = gm%
Hct = %
RBC = millions
Na+, K+, CL-, HCO3-, Ca++ = meq/l
P, Creatinine = mg%
Thymol Turbidity, SGOT = units
BSP = %
• = No determination on specified date

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MAXIMUM OXYGEN INTAKE
TREADMILL

| Subject | Medium | 6 MPH - 8% GRADE | | | | 6 MPH - 10% GRADE | | | | 6 MPH - 12% GRADE | | | | 7 MPH - 8% GRADE | | | | 7 MPH - 10% GRADE | | | | 7 MPH - 12% GRADE | | | | 8 MPH - 8% GRADE | | | | 8 MPH - 10% GRADE | | | |
| | | MOI | | O2/LBM | | MOI | | O2/LBM | | MOI | | O2/LBM | | MOI | | O2/LBM | | MOI | | O2/LBM | | MOI | | O2/LBM | | MOI | | O2/LBM | | MOI | | O2/LBM | |
		B	BR	B	BR	B	BR	B	BR	B	BR	B	BR	B	BR	B	BR	B	BR	B	BR	B	BR	B	BR	B	BR	B	BR	B	BR	B	BR
B B	Silicone	2.95	2.92	49.8	52.1	2.81	3.05	47.4	54.5	2.89		48.9		3.12		54.4																			
	Bedrest	3.36	2.99	56.6	54.9	3.60	3.01	62.7	55.3	2.74		47.7																							
L B	Silicone	3.25	2.44	68.6	53.1	2.73	2.95	57.7	64.2	2.21		46.5		2.61		55.1																			
	Bedrest	2.29	2.39	45.8	47.5	2.30	2.38	46.0	47.3	2.52		52.5																							
E H	Silicone	3.87	3.05	65.4	53.0	5.18	3.79	89.0	65.8	5.23	3.73	90.6	64.8									3.85		62.0		4.23		72.7		3.40		58.4	
	Bedrest	2.81	3.46	47.2	57.6	3.25	3.49	54.6	58.1	3.05	3.88	51.2	64.6							64.0	65.3			59.5									
J R	Silicone	3.63	3.37	68.7	67.2	3.47	5.37	65.7	105.9	3.69		70.0		4.14		78.3		3.81	3.95			3.54													
	Bedrest	2.56	3.43	50.7	68.6	3.68	3.34	76.9	66.7	4.82		95.6																							
B I	Silicone		2.99		47.6	3.26	3.86	51.7	61.3	4.03		63.9		4.99		65.5		3.50		55.5															
	Bedrest	3.85	3.57	66.7	59.2	4.30	3.59	74.5	59.6	4.98	6.08	86.3	101.0					4.22		73.2															
G K	Silicone	3.71		59.3		5.08		81.3																											
	Bedrest	•		•																															
L L	Silicone	3.90	3.39	61.3	53.6	4.36	3.83	68.6	60.6	4.54		71.3		4.07		64.0		3.98		67.8															
	Bedrest	3.55	3.81	60.5	62.4	4.23	3.95	72.0	64.8	3.01	4.12	51.2	68.7	4.19		71.5																			
R M	Silicone		•		•	3.34		45.8		3.53		48.5						3.69		50.7															
	Bedrest	4.27	2.82	56.9	39.5	4.49	3.96	59.8	55.4	5.89	3.90	78.5	54.6													4.32		57.7		4.23		56.4	
B S	Silicone	3.43	3.34	56.5	54.4	4.14	3.84	68.1	62.6	3.93		64.7						3.69		50.7															
	Bedrest	3.61	2.91	56.6	46.2	3.47	3.48	54.3	55.3	3.95		62.0		4.19		65.7		3.97		62.3															
L S	Silicone	3.46	3.12	56.5	52.3	4.11	3.33	67.0	55.8	4.58	3.56	74.6	59.8	3.73	3.35	60.9	56.2	4.31	3.60	70.4	60.5												
	Bedrest	2.87	3.10	46.7	50.1	3.01	2.93	48.9	47.4	3.18	3.60	51.5	58.2					3.50		56.8															
W W	Silicone	3.52	3.55	56.7	58.3	4.18		67.3		4.39	4.15	70.7	68.1	4.62		74.4		4.12	4.10	66.4	67.3	4.32		69.7									
	Bedrest	3.84	3.12	59.3	48.8	4.07	4.57	62.7	71.2	4.52	3.89	69.8	60.8	3.94	3.89	50.7	50.8	4.90		75.6		4.59		70.7		3.44		53.1					

MOI = Maximum Oxygen Intake = L/Min

O2/LBM = Oxygen Consumed/Lean Body Mass = mL/Min/KGM

All Values Corrected to BTPS

B = Baseline

BR = Baseline - Recovery

• = Subject Withdrawn from Program

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SUBJECT	MEDIUM	Dates and Methods of Determinations											
		B-3	T-1	T-2	T-3	T-4	T-5	T-6	T-7	T-8	T-9	T-10	ER-2
		Resp.	D.B.	Resp.	D.B.	Resp.	D.B.	Resp.	D.B.	D.B. / Resp.	D.B. / Resp.	D.B. / Resp.	D.B.
B B	Silicone Bedrest		0.27	0.29	0.31	0.33	0.26	0.40	0.29	/ 0.32	0.26 /	/ 0.29	
L B	Silicone Bedrest		0.21	0.24	0.22	0.21	0.22	0.24	0.23	/ 0.25	0.23 /	/ 0.26	
E H	Silicone Bedrest		0.29	0.34	0.27	0.31	0.32	0.31	0.29	/ 0.28	0.32 /	/ 0.28	
J H	Silicone Bedrest	0.30	0.276 / 0.34	0.31	0.288 / 0.30	0.293 / 0.31	0.261 / 0.27	0.311 / 0.29	0.267	0.27 / 0.266 / 0.31	0.308 / 0.35	0.25 / 0.320	0.27
B I	Silicone Bedrest		0.31	0.32	0.29	0.38	0.31	0.31	0.32	/ 0.29	0.34 /	/ 0.32	
G K	Silicone Bedrest	0.32	0.36	0.27	0.34	0.35	●		●	● /	● /	/ ●	●
L L	Silicone Bedrest	0.32	0.333 / 0.32	0.33	0.229 / 0.30	0.311 / 0.32	0.302 / 0.41	0.348 / 0.34	0.284	0.31 / 0.348 / 0.35	0.288 / 0.36	0.28 / 0.367	0.30
R M	Silicone Bedrest		0.28	0.29	0.27	0.39	0.26	0.51	0.27	/ 0.28	● /	● /	●
B S	Silicone Bedrest	0.30	0.29 / 0.265	0.30	0.30 / 0.270	0.28 / 0.298	0.29 / 0.285	0.28 / 0.328	0.290	0.30 / 0.27 / 0.264	0.276 / 0.29	0.28 / 0.298	0.29
L S	Silicone Bedrest		0.26	0.32	0.23	0.35	0.23	0.31	0.27	/ 0.27	0.27 /	/ 0.32	
W W	Silicone Bedrest	0.35	0.31 / 0.293	0.33	0.31 / 0.288	0.32 / 0.319	0.34 / 0.285	0.32 / 0.315	0.295	0.37 / 0.35 / 0.326	0.274 / 0.38	0.31 / 0.347	0.28

Entries are in L/Min.

All entries corrected to BTPS

D.B. - Douglas bags utilized for determinations

Resp. - Collins respirometer utilized for determinations

B - Baseline

ER - Baseline-Recovery

● - Subject withdrawn from program

SERUM ELECTROPHORESIS

SUBJECT	MEDIUM	DATE OF DETERMINATION																				
		Baseline							T-5							T-10						
		Total Protein	Albumin	Globulins				A/G Ratio	Total Protein	Albumin	Globulins				A/G Ratio	Total Protein	Albumin	Globulins				A/G Ratio
				Alpha 1	Alpha 2	Beta	Gamma				Alpha 1	Alpha 2	Beta	Gamma				Alpha 1	Alpha 2	Beta	Gamma	
BB	Silicone	6.7	4.4	0.3	0.5	0.9	0.6	2.0	7.4	5.2	0.3	0.5	0.9	0.5	2.4	6.8	4.4	0.3	0.6	0.8	0.7	1.8
	Bed Rest	6.5	4.8	0.3	0.4	0.6	0.4	2.9	6.3	4.8	0.2	0.5	0.7	0.7	2.3	6.7	4.5	0.3	0.6	0.7	0.6	2.1
LB	Silicone	8.4	5.6	0.3	0.5	1.1	0.9	2.0	8.3	5.5	0.2	0.5	1.1	1.0	1.9	7.7	3.9	0.3	0.9	1.5	1.1	1.1
	Bed Rest	8.0	5.1	0.2	0.4	1.2	1.1	1.7	8.7	5.7	0.3	0.6	1.1	1.0	1.9	8.3	4.4	0.4	0.7	0.8	1.3	1.1
EH	Silicone	7.5	4.9	0.2	0.5	1.0	0.9	1.9	8.1	5.7	0.2	0.6	0.9	0.7	2.1	8.0	4.9	0.3	0.6	1.1	1.1	1.5
	Bed Rest	6.9	4.8	0.2	0.5	0.7	0.7	2.4	7.9	4.7	0.2	0.6	1.1	1.3	1.5	7.9	5.0	0.2	0.7	1.1	0.9	1.7
JH	Silicone	7.6	6.0	0.2	0.4	0.6	0.4	3.7	8.1	5.7	0.3	0.5	0.8	0.8	2.4	7.8	5.3	0.3	0.6	0.8	0.8	2.0
	Bed Rest	7.6	5.1	0.3	0.6	0.8	0.8	2.1	7.7	5.3	0.3	0.5	0.8	0.8	2.2	7.5	4.9	0.2	0.6	0.8	1.0	1.9
BI	Silicone	7.3	4.9	0.3	0.5	0.8	0.8	2.0	7.9	5.1	0.3	0.7	0.9	0.9	1.8	7.9	5.2	0.3	0.6	0.9	0.9	1.8
	Bed Rest	6.8	4.3	0.3	0.5	0.8	0.9	1.8	7.4	5.1	0.3	0.4	0.8	0.8	2.3	7.7	4.9	0.3	0.5	0.8	1.2	1.7
GK	Silicone	7.8	5.2	0.3	0.5	1.0	0.8	2.0	7.5	5.1	0.2	0.6	0.8	0.8	2.1	•	•	•	•	•	•	•
	Bed Rest	8.0	5.3	0.2	0.6	0.9	1.0	1.9	•	•	•	•	•	•	•	•	•	•	•	•	•	•
LL	Silicone	7.2	5.1	0.2	0.4	0.7	0.8	2.5	6.9	4.7	0.2	0.6	0.7	0.7	2.2	7.5	4.8	0.3	0.6	1.1	0.7	1.8
	Bed Rest	6.8	4.9	0.3	0.4	0.5	0.6	2.6	6.7	4.5	0.3	0.5	0.7	0.6	2.1	6.7	4.5	0.2	0.5	0.8	0.7	2.1
RM	Silicone	7.1	5.2	0.2	0.4	0.6	0.7	2.8	7.0	5.1	0.3	0.3	0.7	0.6	2.6	6.9	4.5	0.3	0.5	0.7	0.9	1.9
	Bed Rest	7.2	5.3	0.3	0.3	0.6	0.7	2.7	7.1	5.2	0.3	0.3	0.7	0.6	2.8	7.5	5.0	0.3	0.5	0.8	0.9	1.9
BS	Silicone	7.6	4.5	0.4	0.6	1.0	1.1	1.5	7.5	4.7	0.3	0.4	0.9	1.1	1.9	7.4	5.0	0.2	0.5	0.8	0.9	2.1
	Bed Rest	8.1	5.7	0.2	0.4	0.8	1.0	2.5	7.2	4.5	0.2	0.5	0.9	0.8	2.0	7.4	5.0	0.2	0.4	0.9	0.9	2.0
LS	Silicone	6.4	4.7	0.2	0.2	0.7	0.6	2.8	7.3	5.3	0.2	0.3	0.7	0.8	2.4	6.9	4.1	0.4	0.6	0.9	0.9	1.5
	Bed Rest	7.1	4.5	0.4	0.5	0.8	0.9	1.7	7.5	4.7	0.4	0.5	0.9	1.0	1.7	7.4	5.1	0.3	0.4	0.5	0.8	2.1
WW	Silicone	6.9	4.9	0.2	0.4	0.7	0.7	2.4	7.4	5.3	0.2	0.5	0.8	0.8	2.2	7.0	5.0	0.2	0.5	0.7	0.6	2.5
	Bed Rest	7.6	5.4	0.2	0.4	0.7	0.9	2.4	7.2	4.9	0.3	0.5	0.9	0.7	2.1	7.5	5.4	0.3	0.5	0.7	0.6	2.0

Entries are in gms% except for A/G Ratio
• = Subject withdrawn from program

URINE CHEMISTRIES

Subjects and Dates of Determinations

(Values given as Silicone / Bedrest where both appear.)

Subject B B

TEST	MEDIUM	B-2	B-3	T-1	T-2	T-3	T-5	T-6	T-7	T-8	T-9	T-10	BR-1	BR-2
Specific Gravity	Silicone / Bedrest	1.012			1.016	1.014 1.014	1.020 / 1.012	1.012		1.012 / 1.018		1.010		
pH	Silicone / Bedrest	6.6 / 6.4	7.0		6.8 / 6.0	6.4	6.0 / 6.0	6.8		6.4 / 6.5	6.8	6.0		
Osmolality	Silicone / Bedrest	475 / 524	491	427	460 / 521	532	505 / 595	540		636 / 520	419			525
Sodium	Silicone / Bedrest	162 / 116	151	171	194 / 130	98	116 / 125	56		182 / 107	131			75
Potassium	Silicone / Bedrest	52 / 91	76	76	81 / 103	122	93 / 112	51		88 / 75	88			54
Calcium	Silicone / Bedrest	7.1 / 4.4	6.6	9.6	7.4 / 6.4	8.0	6.3 / 8.1	3.8		11.0 / 9.2	8.8			5.7
Chloride	Silicone / Bedrest	161 / 143	138	183	198 / 157	135	97 / 147	68		196 / 103	166			94
Phosphorus	Silicone / Bedrest	0.89 / 0.36	0.57	0.68	1.1 / 0.71	0.98	1.1 / 1.1	0.46		1.2 / 0.76	0.90			0.56
Creatinine	Silicone / Bedrest	1510 / 1298	1863	1595	1504 / 1440	1800	1900 / 2230	885		2170 / 1885	1658			1245
17-Hydroxy-Ketosteroids	Silicone				12.1	8.0				12.0		6.8		
Epinephrine	Silicone				5.5	10.5				10.5		1.7		
Nor-epinephrine	Silicone				27.6	35.9				50.0		57.7		

PSP (Silicone) — B-2: 15 Min 41, 30 Min 17, 60 Min 18, 120 Min 13, TOTAL 89. BR-2: 15 Min 39, 30 Min 12, 60 Min 18, 120 Min 14, TOTAL 84.

Subject L B

TEST	MEDIUM	B-1	B-2	B-3	T-1	T-2	T-3	T-5	T-6	T-7	T-8	T-9	T-10	BR-1	BR-2
Specific Gravity	Silicone / Bedrest		1.022			1.021 / 1.021	1.028	1.022 / 1.019			1.019 / 1.020	1.024		1.012	
pH	Silicone / Bedrest		6.8	5.9		6.0 / 5.5	6.0	6.0 / 6.0	6.8		6.0 / 6.4	6.0		6.0	
Osmolality	Silicone / Bedrest		810	701	849	773 / 760	918	570 / 878	566		738 / 633	775		560	
Sodium	Silicone / Bedrest		146	59	157	109 / 137	124	92 / 118	92		121 / 164	79		91	
Potassium	Silicone / Bedrest		27	31	45	73 / 89	71	80 / 68	48		80 / 45	52		74	
Calcium	Silicone / Bedrest		7.6	4.3	11	8.5 / 11	9.2	12.0 / 7.4	5.0		12.0 / 11.0	7.8		9.6	
Chloride	Silicone / Bedrest		149	47	176	127 / 191	153	122 / 124	100		122 / 162	104		107	
Phosphorus	Silicone / Bedrest		0.67	0.57	0.49	0.78 / 0.74	1.1	1.2 / 0.83	0.57		1.01 / 0.76	0.60		0.85	
Creatinine	Silicone / Bedrest		1025	960	1428	1640 / 1600	1660	1890 / 1392	832		1880 / 1675	1090		1345	
17-Hydroxy-Ketosteroids	Bedrest										7.9	3.9	8.1	6.4	
Epinephrine	Bedrest								5.5		8.8	18.2	15.3		
Nor-epinephrine	Bedrest								16.3		22.0	22.9	30.7		

PSP (Silicone) — B-1: 39/17/15/9.1, TOTAL 80. B-2: 15/10/16/21, TOTAL 62. BR-1: 45/26/17/12, TOTAL 100. BR-2: 7.9/44/22/10, TOTAL 84.

Subject E H

TEST	MEDIUM	B-1	B-2	B-3	T-1	T-2	T-3	T-5	T-6	T-7	T-8	T-9	T-10	BR-1	BR-2
Specific Gravity	Silicone / Bedrest		1.016			1.031 / 1.018	1.025	1.027 / 1.027			1.008 / 1.025	1.018		1.008	
pH	Silicone / Bedrest		6.4 / 6.6	5.9		6.4 / 6.7	6.0	6.0 / 6.8	6.8		6.5 / 6.4	6.4		6.5	
Osmolality	Silicone / Bedrest		646 / 612	427	653	919 / 752	912	670 / 561	980		452 / 680	592		440	
Sodium	Silicone / Bedrest		260 / 258	145	155	101 / 148	64	62 / 69	109		133 / 146	155		162	
Potassium	Silicone / Bedrest		93 / 98	64	85	135 / 92	24	95 / 104	87		81 / 69	76		140	
Calcium	Silicone / Bedrest		3.6 / 7.1	9.1	11.0	7.8 / 8.0	7.7	7.5 / 7.9	6.5		12.0 / 11.0	12.0		17.0	
Chloride	Silicone / Bedrest		227 / 280	136	155	146 / 171	96	80 / 95	129		136 / 158	160		185	
Phosphorus	Silicone / Bedrest		1.3 / 1.3	0.76	0.64	1.0 / 0.97	1.1	0.98 / 1.2	0.92		0.93 / 1.2	1.1		1.22	
Creatinine	Silicone / Bedrest		1792 / 1660	1422	1420	1910 / 1400	1548	1510 / 1743	1120		1745 / 1775	1620		2120	
17-Hydroxy-Ketosteroids	Bedrest								6.1	7.6	7.6	7.3			
Epinephrine	Silicone										7.1	7.4	9.2	5.9	
Nor-epinephrine	Silicone										23.8	23.2	20.7	41.8	

PSP (Silicone) — T-8: 36/21/21/16, TOTAL 100. BR-1: 36/29/22/16, TOTAL 100. BR-2: 32/21/16/11, TOTAL 80.

Subject J E

TEST	MEDIUM	B-1	B-2	B-3	T-1	T-2	T-3	T-4	T-5	T-6	T-7	T-8	T-9	T-10	BR-1	BR-2
Specific Gravity	Silicone / Bedrest		1.009	1.012	1.026	1.020	1.028								1.016	
pH	Silicone		5.8	6.0	6.0		6.0		8.0							
Osmolality	Silicone		349	410	593	665	784	672	1265							
Sodium	Silicone		89	200	135	115	77	31	120							
Potassium	Silicone		24	66	70	54	47	69	74							
Calcium	Silicone		12.0	14.0	13.0	7.9	10.0	8.5	13.0							
Chloride	Silicone		94	214	163	123	96	58	88							
Phosphorus	Silicone		0.65	1.6	0.92	0.95	0.96	0.83	0.86							
Creatinine	Silicone		915	2208	1600	1510	1550	1430	1750							
17-Hydroxy-Ketosteroids	Bedrest					8.2	7.0		7.0		6.0	6.5	3.9			
Epinephrine	Silicone / Bedrest					11.0	7.5	4.1 / 3.8	5.1 / 10.4	3.3 / 9.2		11.8 / 14.3				
Nor-epinephrine	Silicone / Bedrest					36.6	44.3	14.9 / 8.9	47.0 / 17.4	53.1 / 17.8		60.4 / 47.9				

Subject B I

TEST	MEDIUM	B-1	B-2	B-3	T-1	T-2	T-3	T-5	T-6	T-7	T-8	T-9	T-10	BR-1	BR-2
Specific Gravity	Silicone / Bedrest		1.027	1.026	1.023 / 1.024	1.023 / 1.025	1.014	1.018 / 1.009	1.019 / 1.020		1.017 / 1.000	1.010		1.006	
pH	Silicone / Bedrest		6.2		6.8 / 5.9	6.8 / 5.9		6.8 / 6.4	6.5 / 6.0		6.0 / 6.8	6.0		6.5	
Osmolality	Silicone / Bedrest		681	884	821	767 / 459	535 / 356	430 / 446	487 / 467	203	547 / 432	352		375	
Sodium	Silicone / Bedrest		29	133	95	172 / 155	74 / 67	17 / 71	133 / 120	136	157 / 55	105		59	
Potassium	Silicone / Bedrest		42	71	45	65 / 51	48 / 76	74 / 41	85 / 65	82	97 / 55	86		54	
Calcium	Silicone / Bedrest		5.9	6.6	8.6	15.0 / 13.0	13.1 / 11.0	13.7 / 8.8	6.8 / 15.0	9.3	22.0 / 15.0	16.0		13.0	
Chloride	Silicone / Bedrest		59	111	85	170 / 151	91 / 85	45 / 139	143 / 55	22	128 / 46	144		72	
Phosphorus	Silicone / Bedrest		1.5	1.2	0.90	0.76 / 0.87	0.82 / 0.83	1.1 / 0.90	1.3 / 2.0	0.82	0.92 / 0.52	1.16		0.52	
Creatinine	Silicone / Bedrest		948	1850	1854	1975 / 1300	1874 / 1050	1112 / 1425	770 / 1540	845	3470 / 2020	1730		1675	
17-Hydroxy-Ketosteroids	Bedrest						7.9		6.5			8.4		1.6	
Epinephrine	Silicone / Bedrest						4.9	14.0	7.2		9.3				
Nor-epinephrine	Silicone / Bedrest						15.6	59.1	24.5		66.7				

PSP (Silicone) — BR-2: 15 Min 30, 30 Min 22, 60 Min 18, 120 Min 12, TOTAL 90. (B-1 column: 47/22/20/15, TOTAL 104.)

Osmolality = mOsm/KG
Sodium, Potassium, Calcium, Chloride = MEQ/24h
Phosphorus = G/24h
Creatinine, 17-Hydroxy Ketosteroids = MGM/24h
Epinephrine, Nor-epinephrine = µG/24h
PSP = % excretion

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URINE CHEMISTRIES

Subjects and Dates of Determination

TEST	MEDIUM	G K											L L												R M											B S												L S										W V											
Specific Gravity	Silicone / Bedrest																																																																				
pH	Silicone / Bedrest																																																																				
Osmolality	Silicone / Bedrest																																																																				
Sodium	Silicone / Bedrest																																																																				
Potassium	Silicone / Bedrest																																																																				
Calcium	Silicone / Bedrest																																																																				
Chloride	Silicone / Bedrest																																																																				
Phosphorus	Silicone / Bedrest																																																																				
Creatinine	Silicone / Bedrest																																																																				
17-Hydroxy-Ketosteroids	Silicone / Bedrest																																																																				
Epinephrine	Silicone / Bedrest																																																																				
Nor-epinephrine	Silicone / Bedrest																																																																				
PSP: 15 Min. 30 Min. 60 Min. 120 Min. TOTAL	Silicone																																																																				

Osmolality = mOsm 1 Kg.
Sodium, Potassium, Calcium, Chloride = MEQ/24h
Phosphorus = G/24h
Creatinine, 17-Hydroxy Ketosteroids = MGM/24h
Epinephrine, Nor-epinephrine = µG/24h
PSP = % excretion
* = Specimen not obtained

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NASA-S-66-5717 JUN 16

$\dfrac{JA}{1\text{-}31\text{-}66}$
70° tilt

Legend:
——— Systalic
—·—·— Diastalic
- - - - - Heart Rate

Y-axis: B.P. (mm Hg) and Heart Rate (Beats / Min.)
X-axis: Time (Min.)

Tilt

$$\frac{JA}{2-11-66}$$
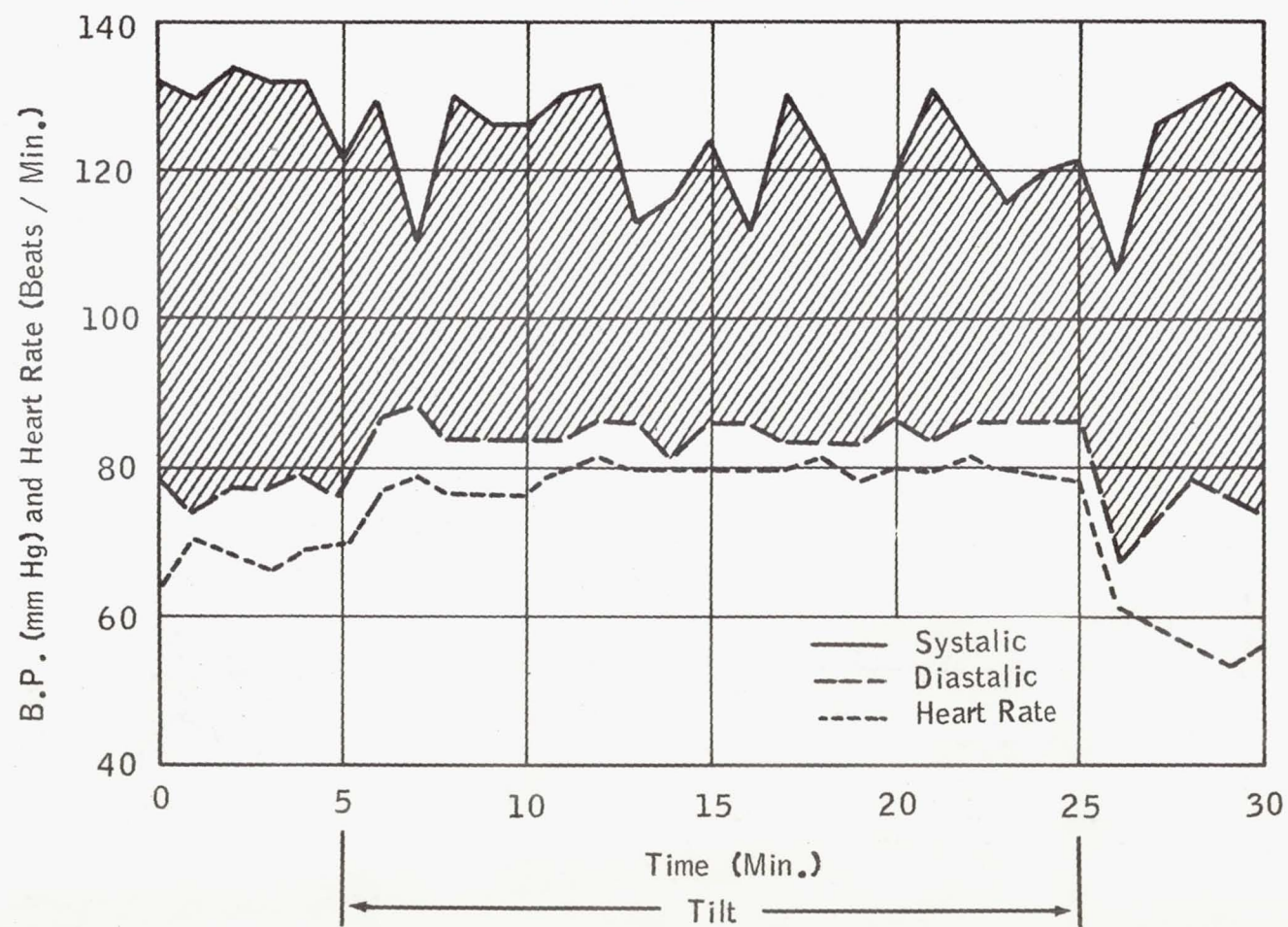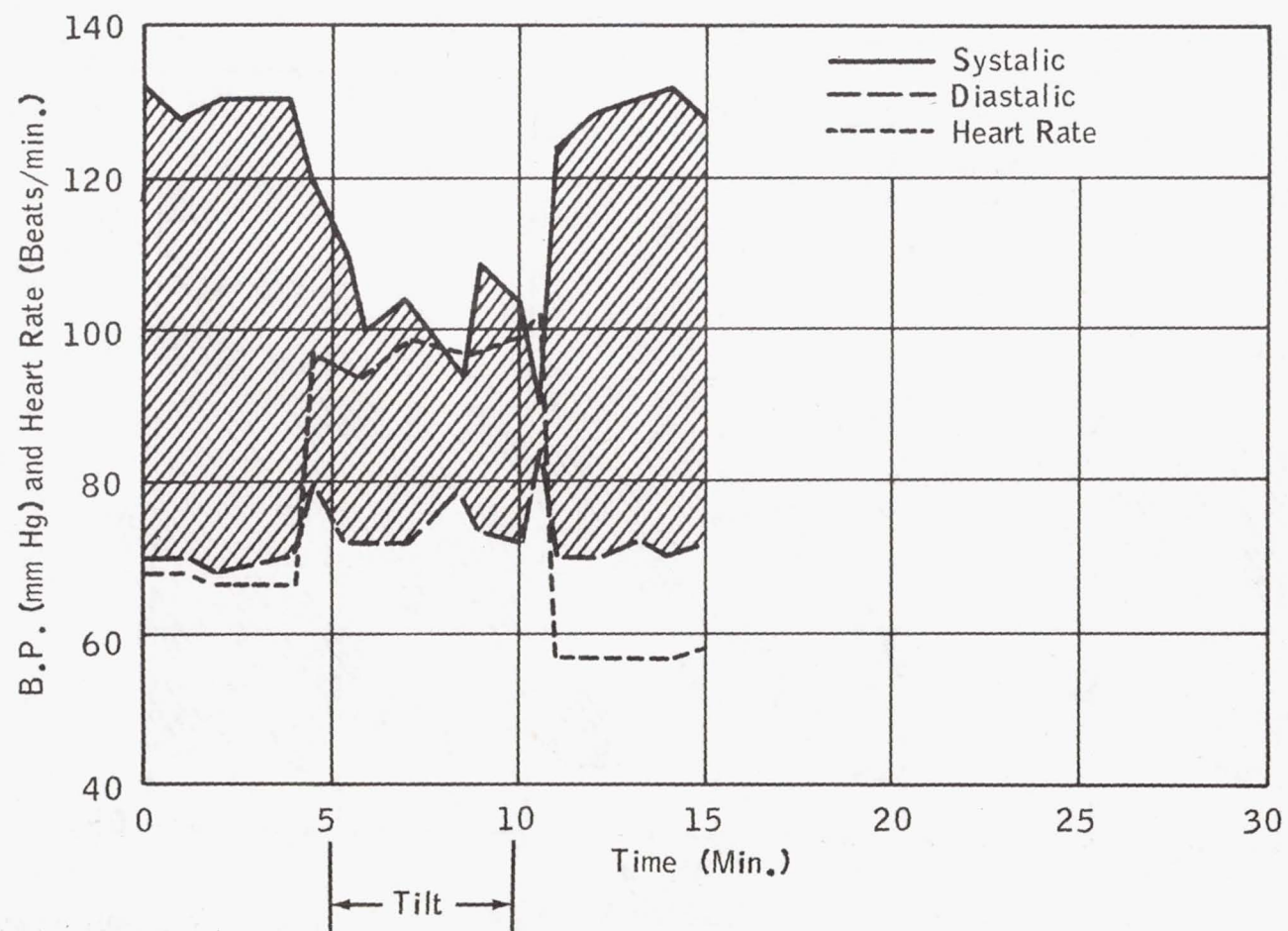
NASA-S-66-5718 JUN 16

$\dfrac{\text{RE}}{\text{1-30-66}}$
70° tilt

$$\frac{RE}{2\text{-}11\text{-}66}$$
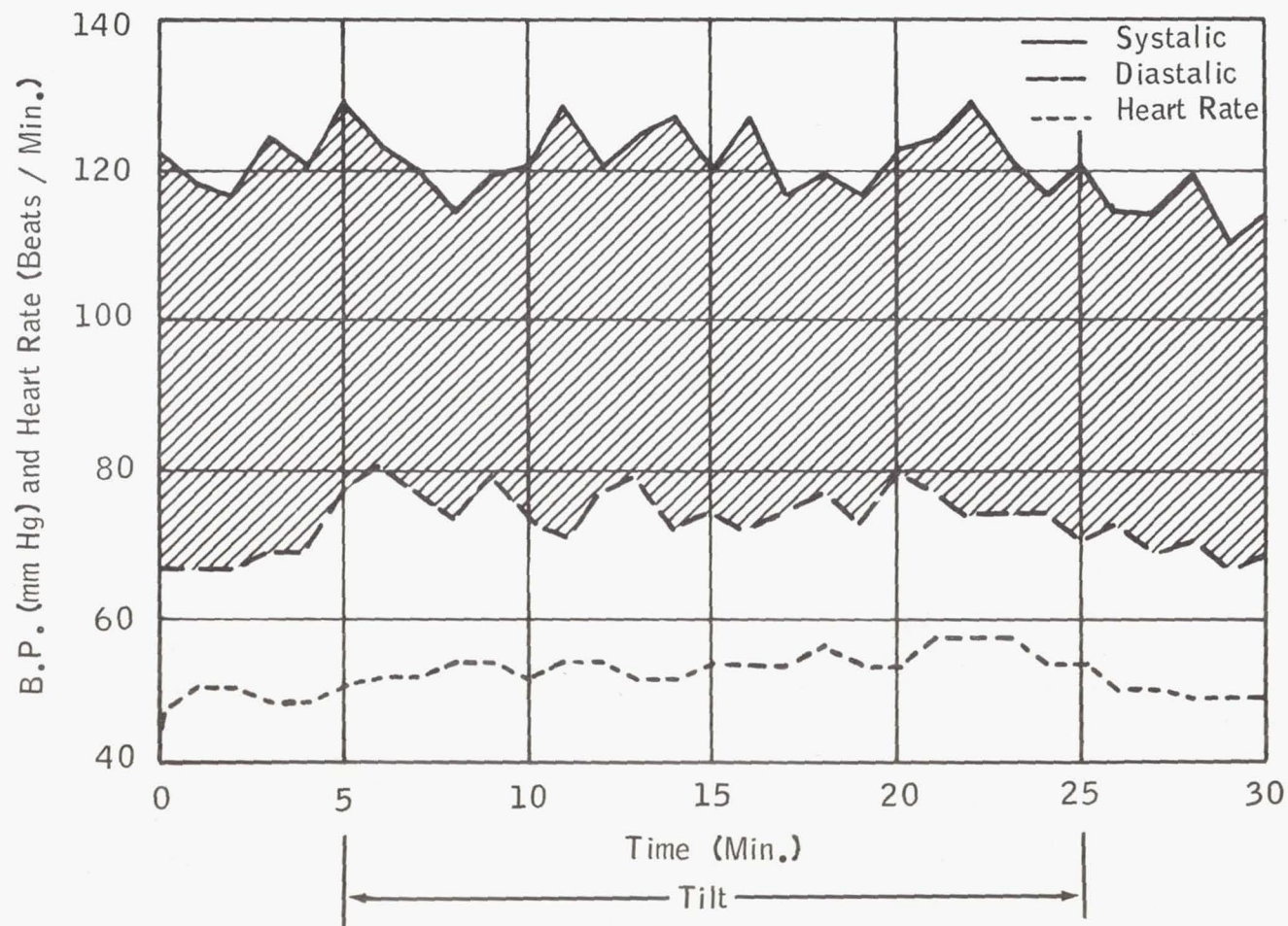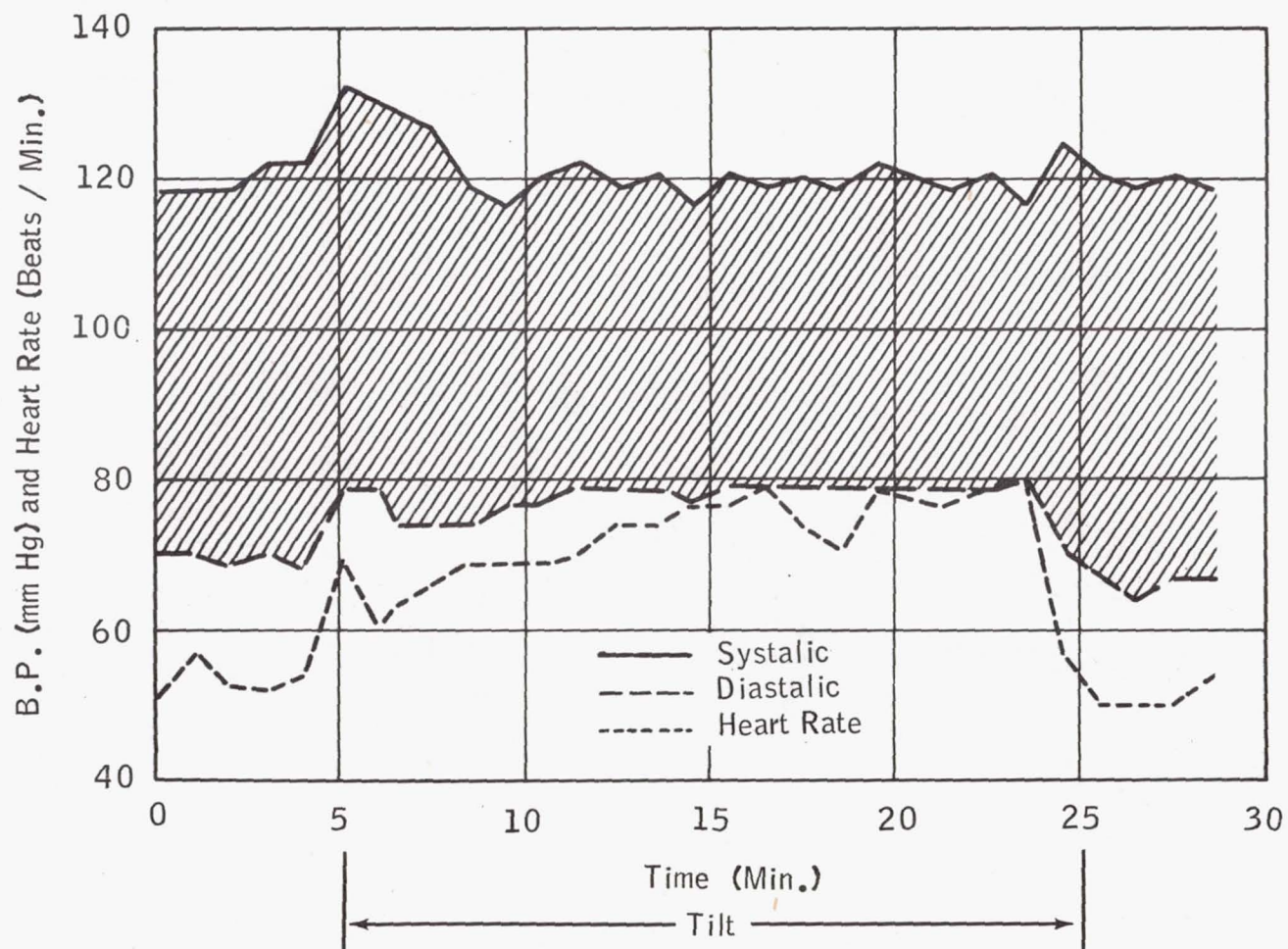
NASA-S-66-5722 JUN 16

$\dfrac{EH}{1-31-66}$

Systalic
Diastalic
Heart Rate
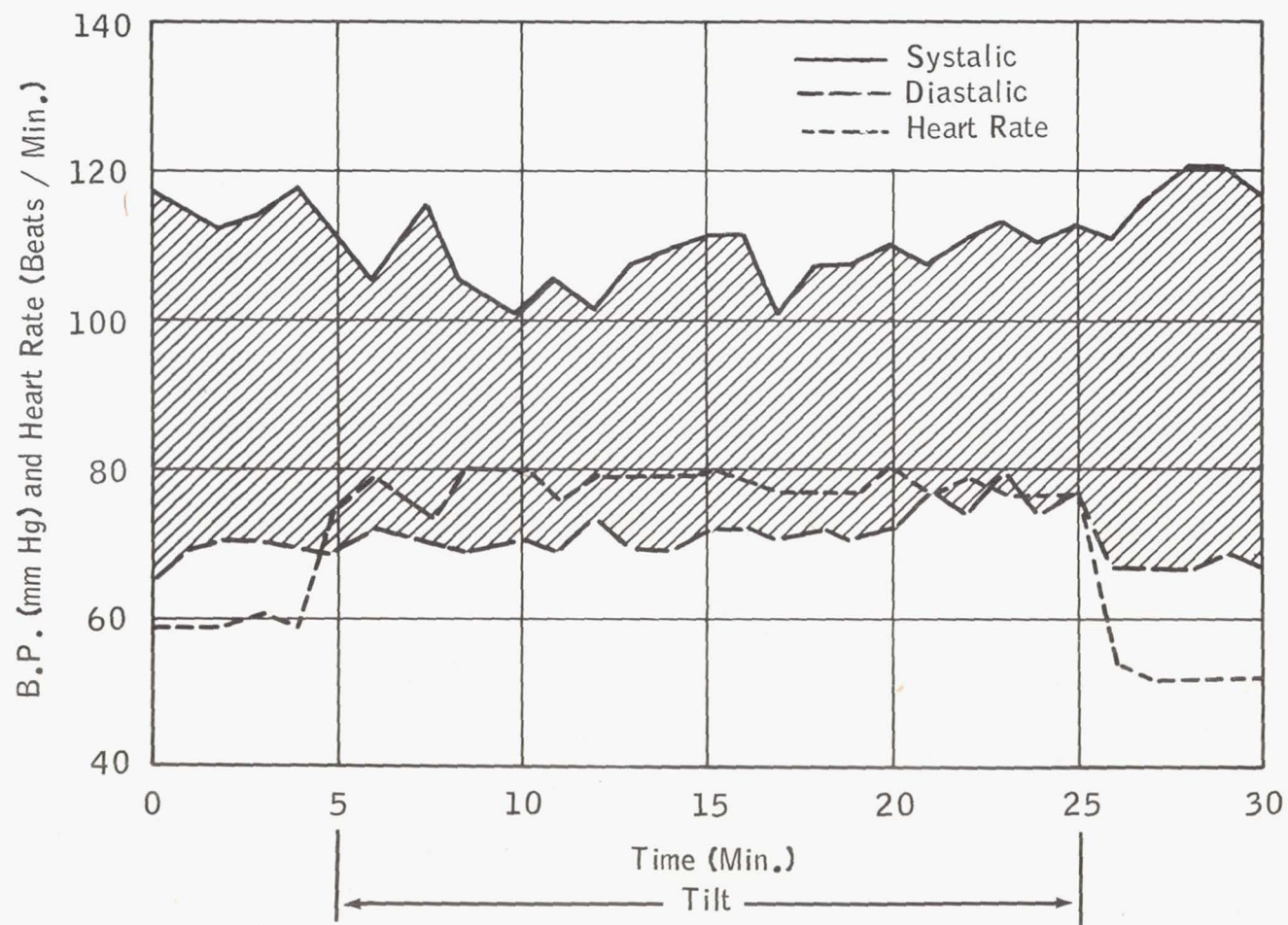
$$\frac{EH}{2\text{-}11\text{-}66}$$
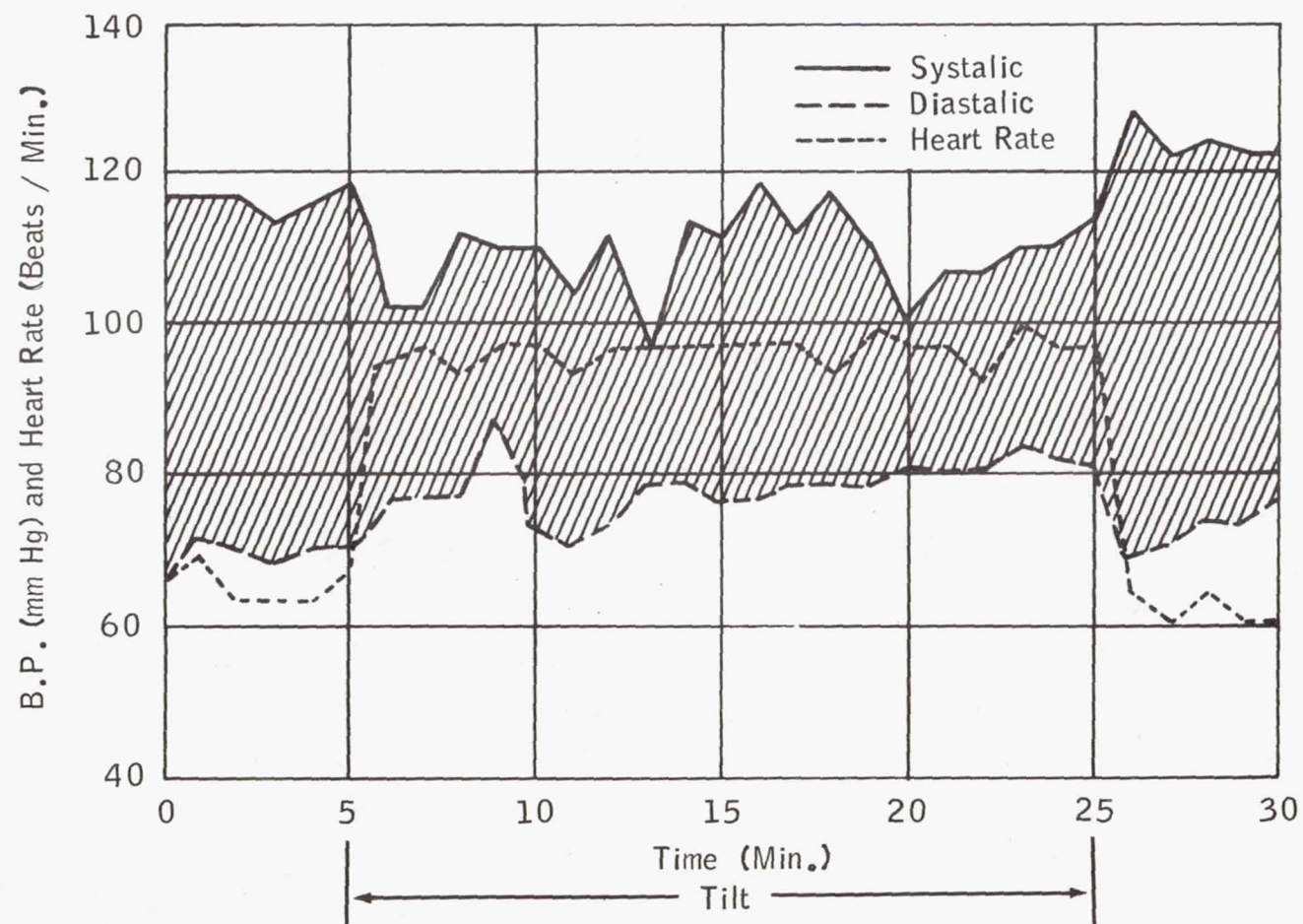
NASA-S-66-5714 JUN 16

$\dfrac{\text{JH}}{\text{1-31-66}}$
70° tilt

Systalic
Diastalic
Heart Rate

B.P. (mm Hg) and Heart Rate (Beats / Min.)

Time (Min.)

Tilt

$$\frac{JH}{2\text{-}11\text{-}66}$$
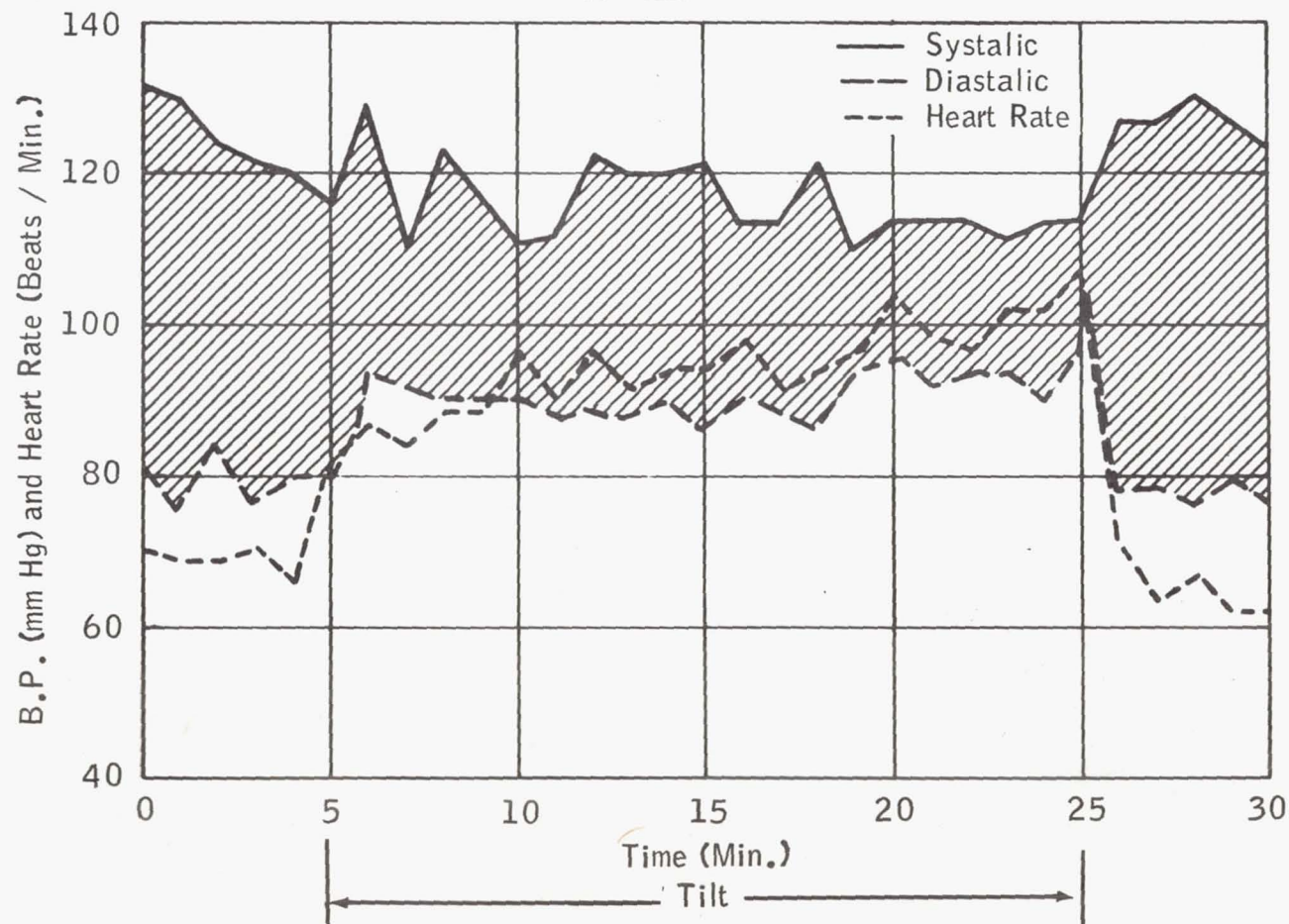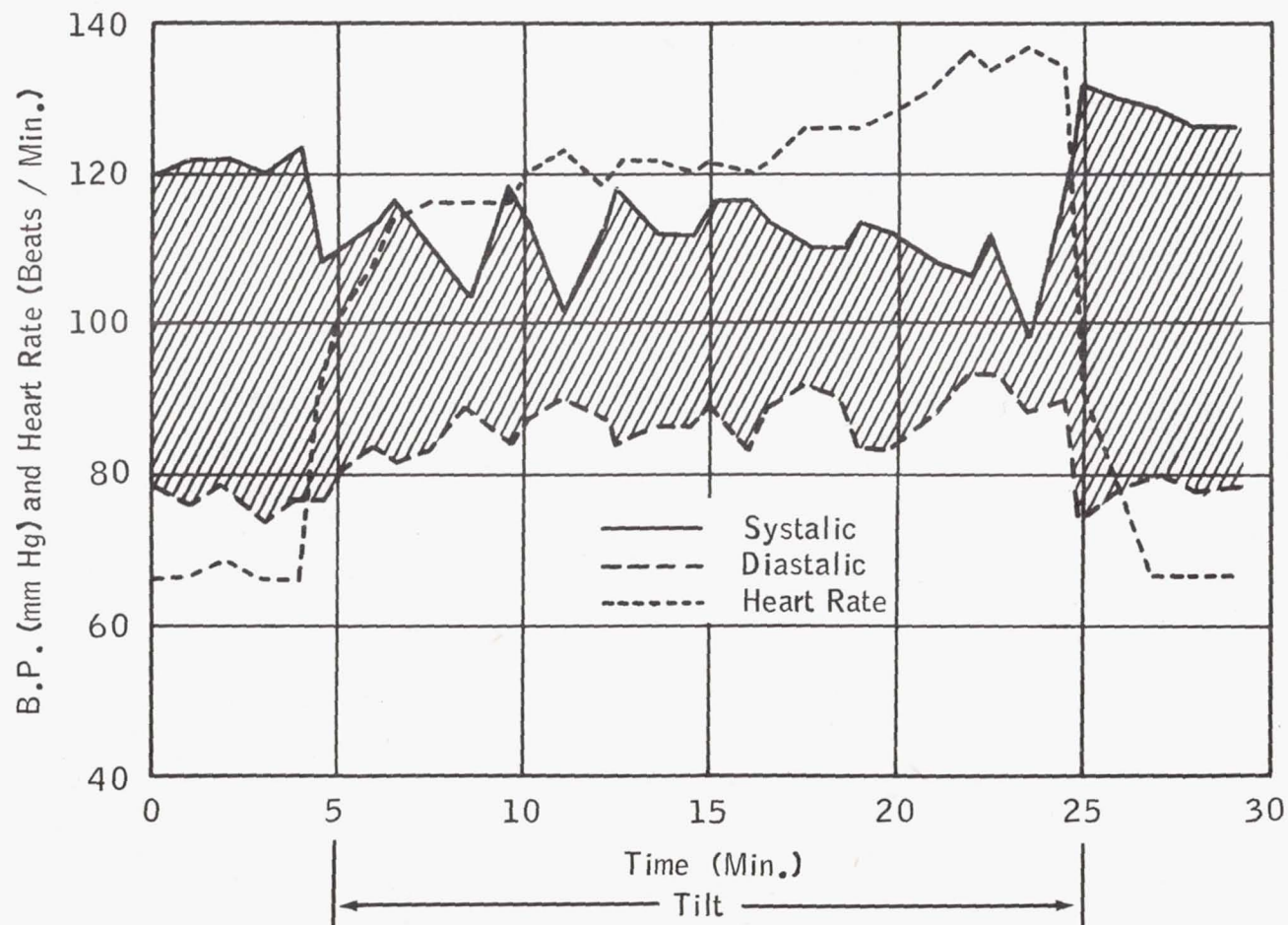
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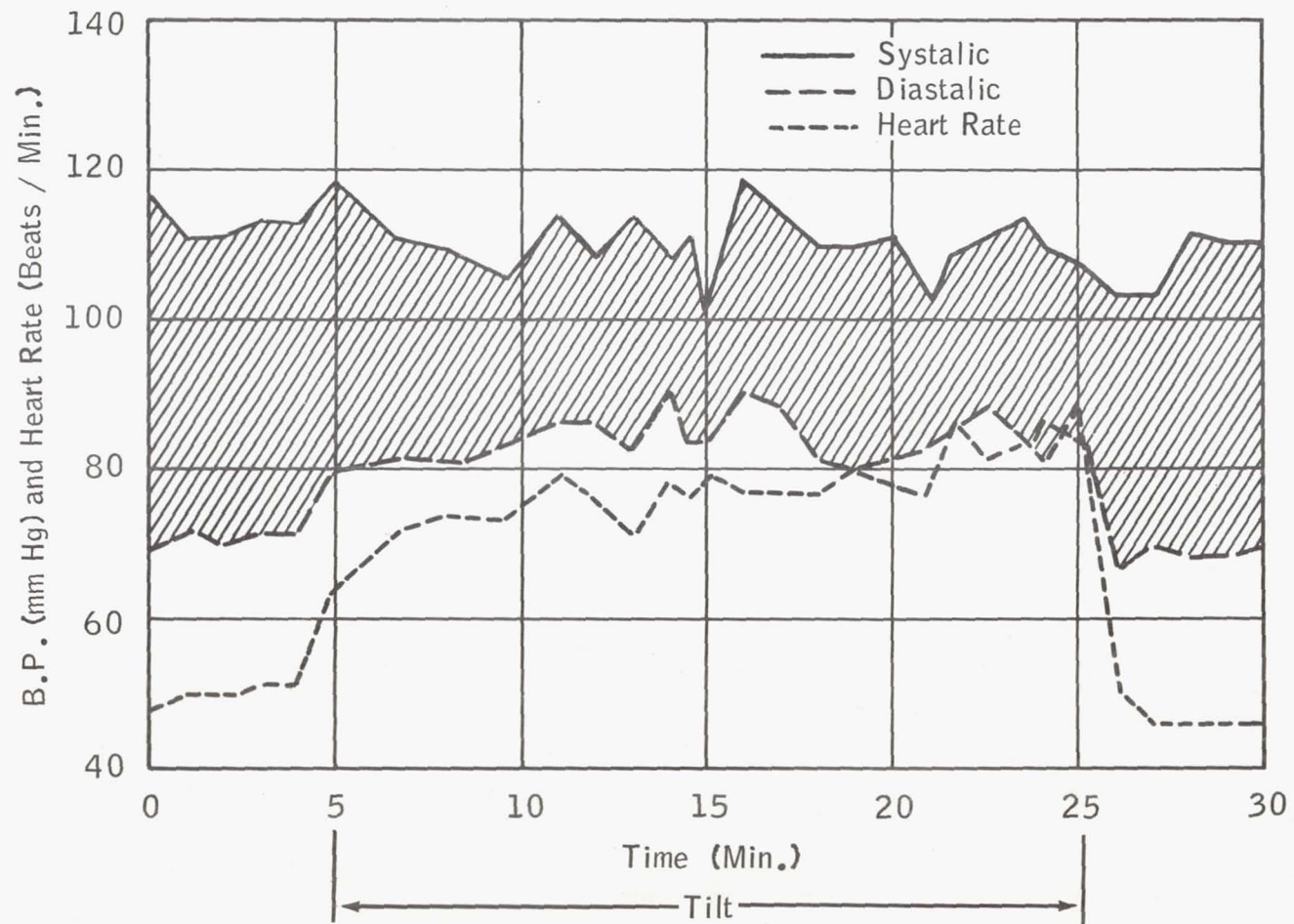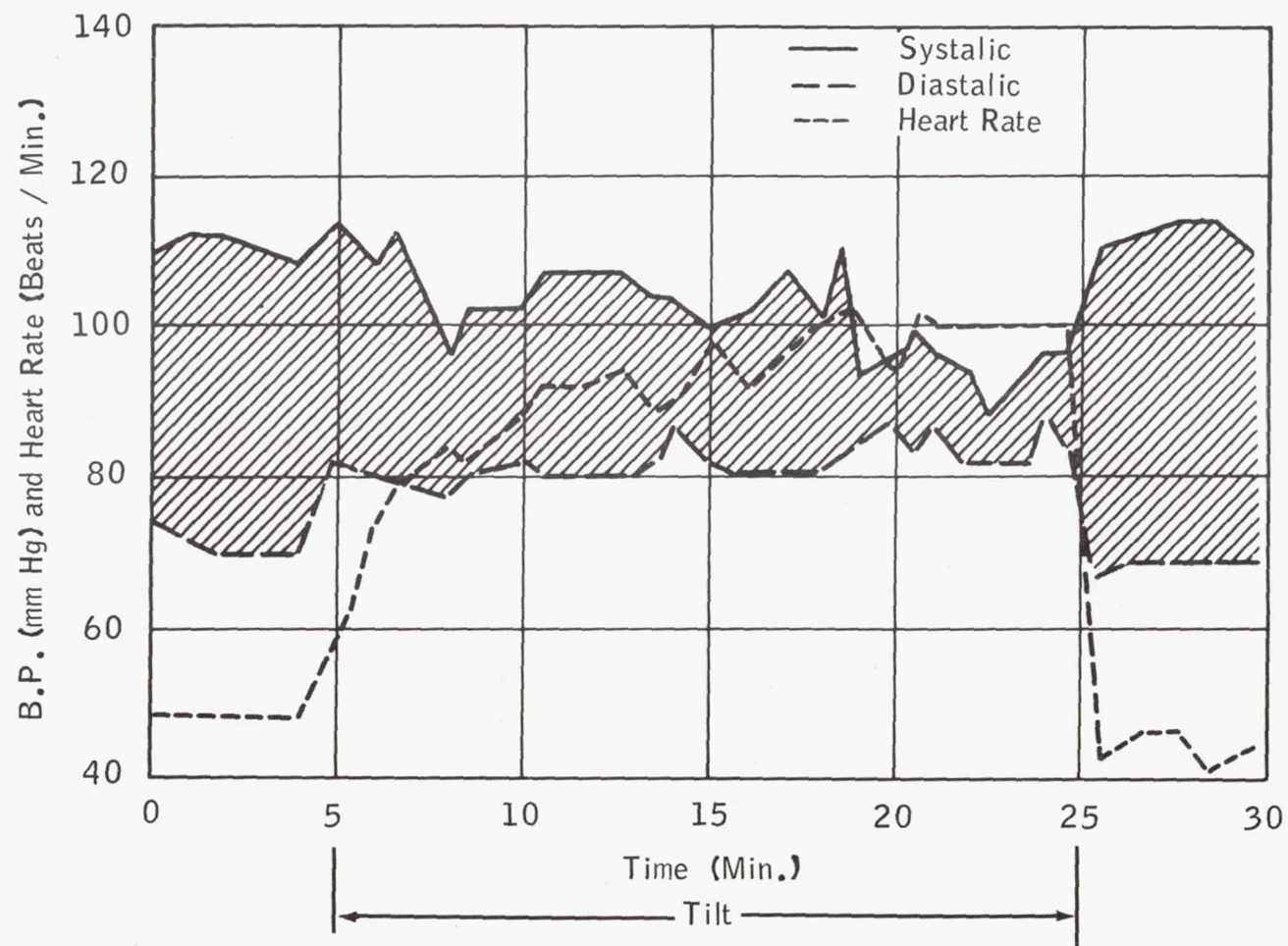
NASA-S-66-5725 JUN 16 $\frac{LL}{1-31-66}$

Figure showing B.P. (mm Hg) and Heart Rate (Beats / Min.) versus Time (Min.) with Systalic, Diastalic, and Heart Rate traces, and a Tilt period marked from 5 to 25 minutes.

$$\frac{LL}{2\text{-}11\text{-}66}$$
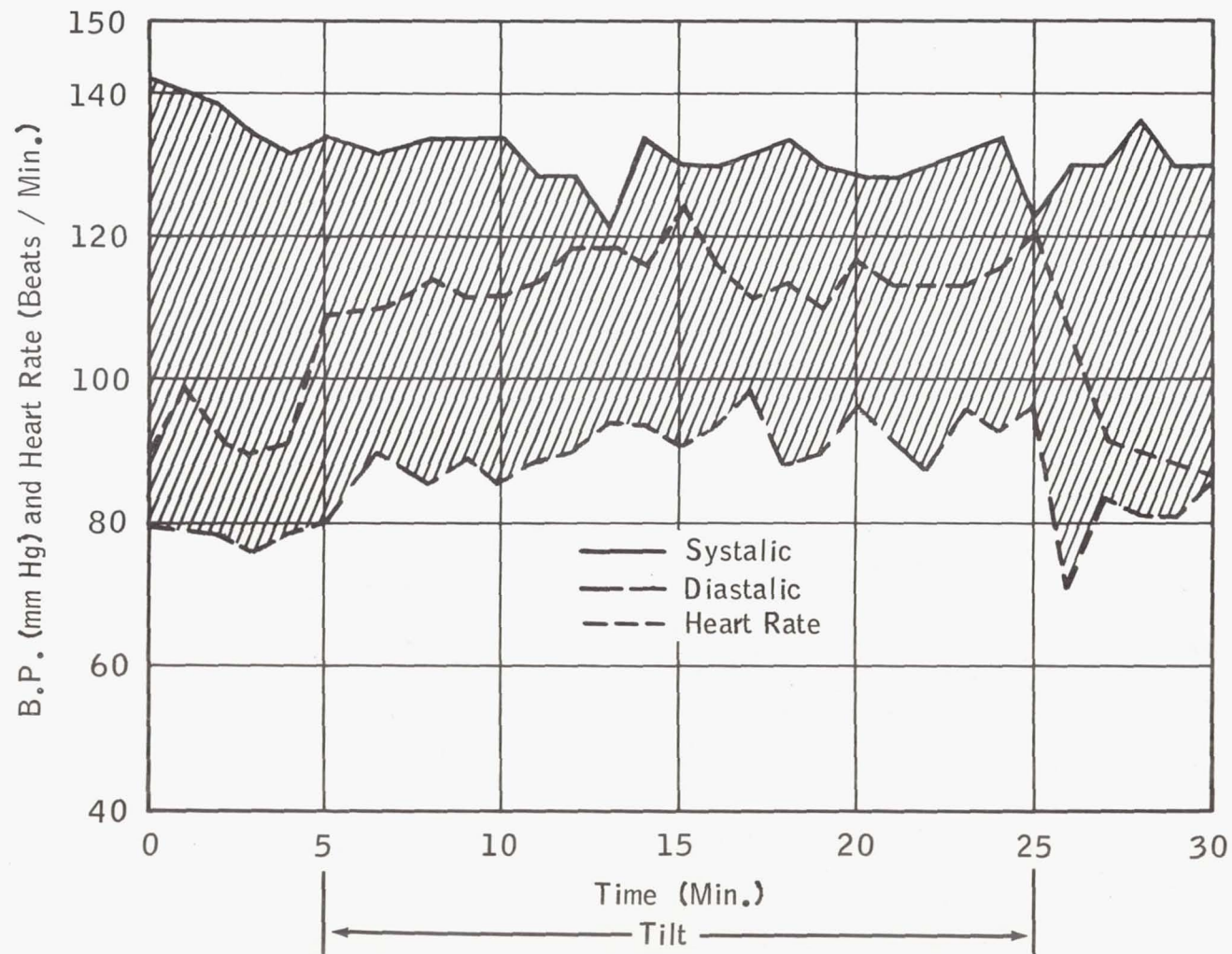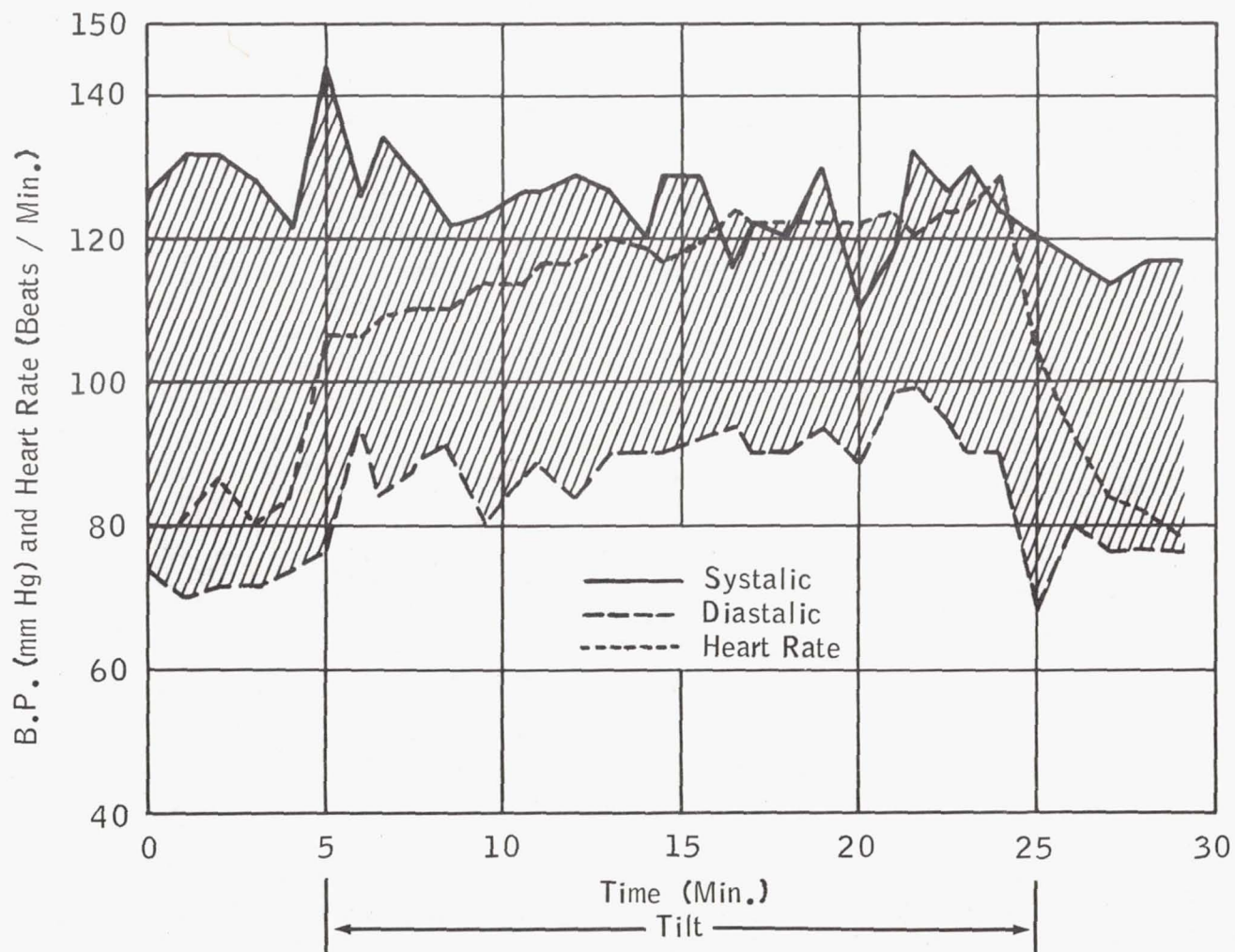
BIO ASSAY STEP FUNCTIONS
TERMINATION POINTS
NULL GRAVITY ANALOGS TASK 3 & 4
1966

SUBJECT	TASK	1-30	1-31	2-2	2-4	2-8	2-9	2-11	2-12	2-13	
ARENS, J.	3	4.0						2.8	3.1	3.5	
EVERETT, R.	3	①5.0						②3.1	3.5	3.5	
LANE, L.	3		3.5					2.8	3.1	3.5	
HALLBERG, J.	3	4.0						3.1	3.1	3.5	
HANSEN, L.	3		4.0					2.8	3.1	3.5	
HOYER, E.	3		3.2					2.8	3.1	3.5	
MAC DOUGAL, R.	4	3.2		2.4	2.4	③	2.35	2.4	3.1	3.1	
WESSBERG, W.	4	4.0		2.4	2.4	2.4	2.4	2.4	2.8	2.8	

The column header $+G_z$ spans the dated columns.

① GREYING OF PERIPHERAL LIGHTS ONLY
② LOST PERIPHERAL LIGHTS ONLY
③ TERMINATED BECAUSE OF NAUSEA

MEASUREMENT OF CARDIOVASCULAR STATUS OF SUBJECTS AT BED REST

TILT-TABLE TEST: Subjects RM and WW

LOWER BODY NEGATIVE PRESSURE: Subjects RM and WW

ACCELERATION TOLERANCE $(+G_z)$: Subjects RM and WW

NASA-S-66-5720 JUN 16
$\dfrac{RM}{1-30-66}$

163

$$\frac{MacDougal}{2\text{-}10\text{-}66}$$
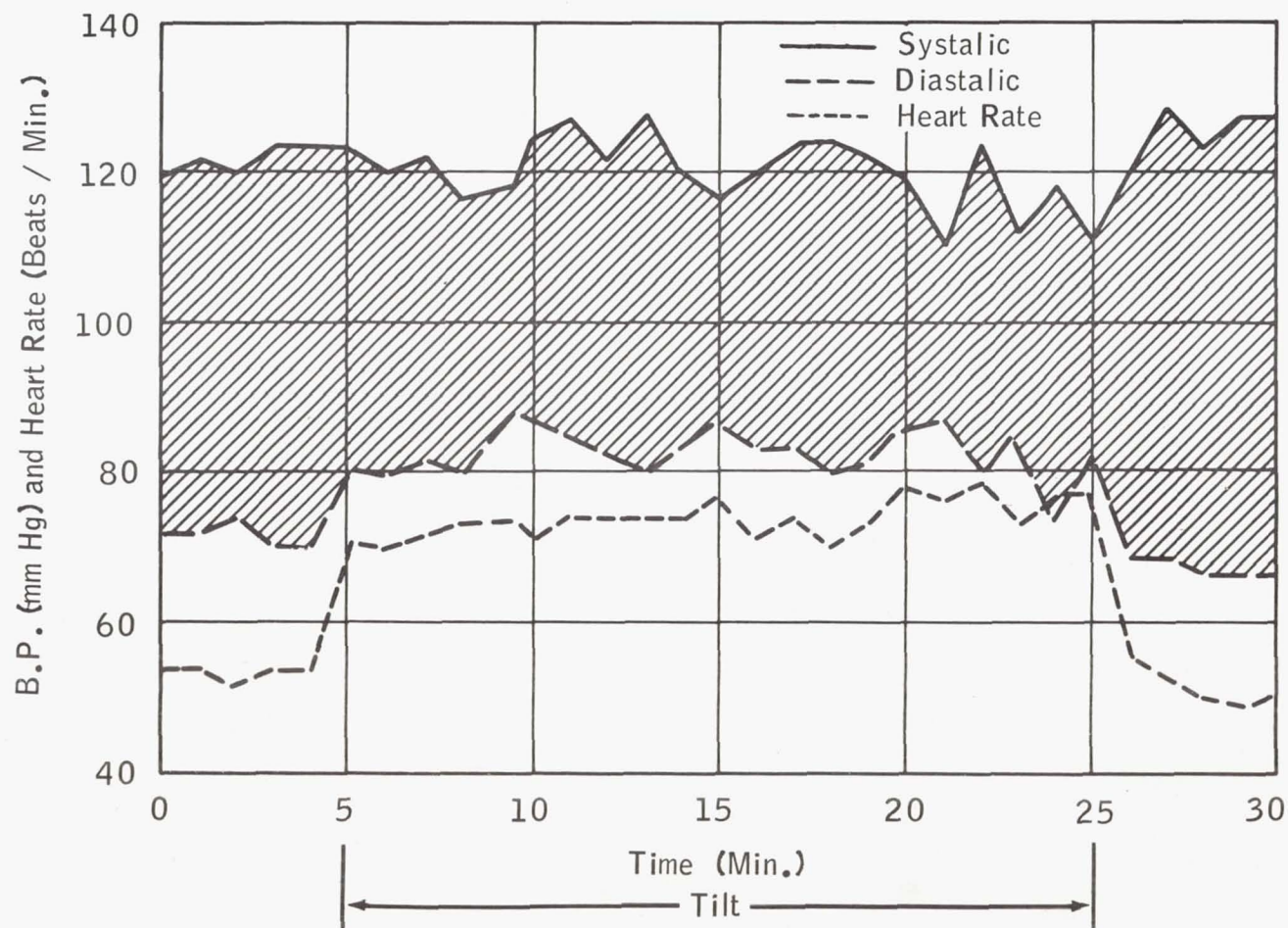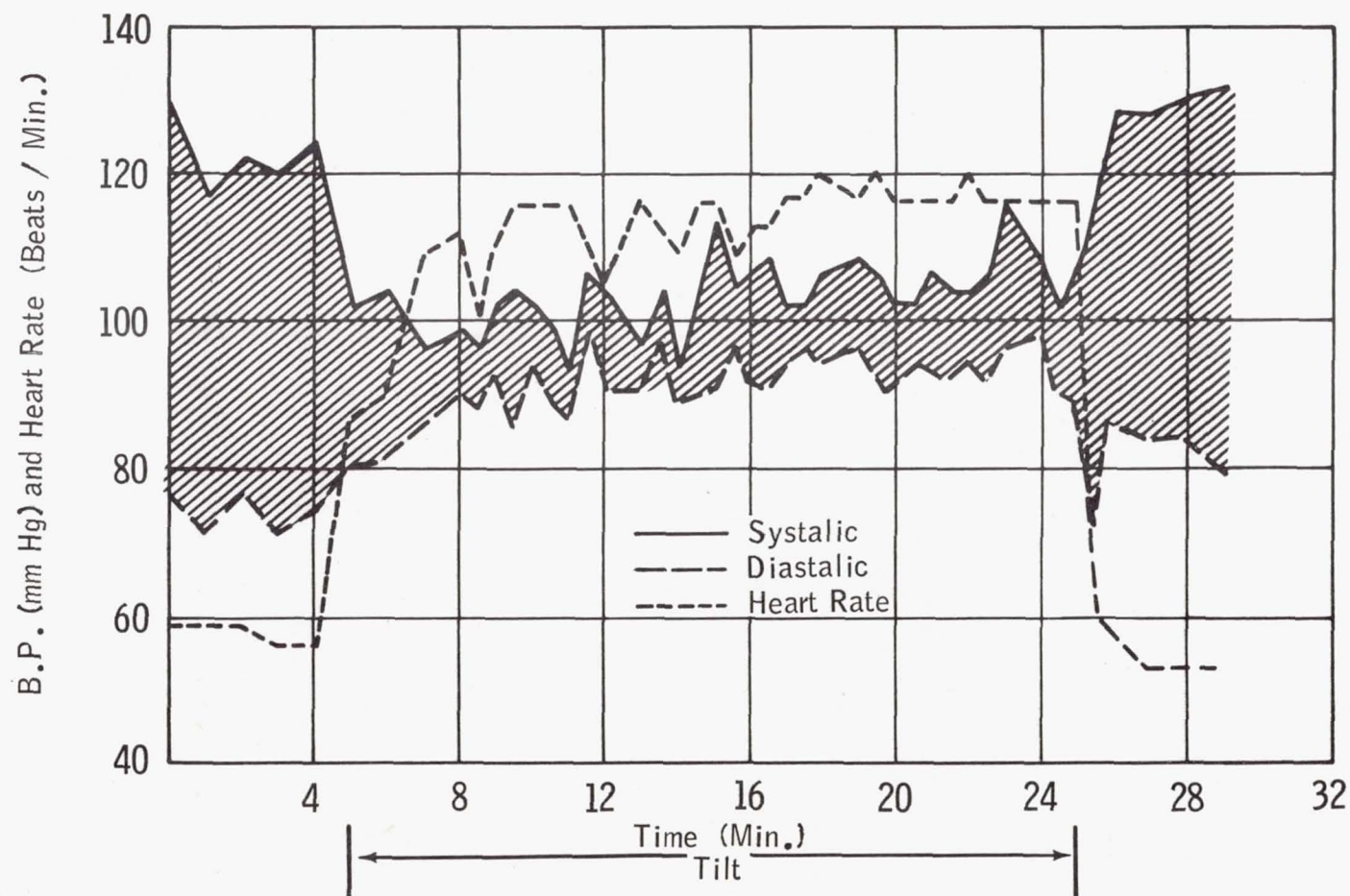
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$$\frac{WW}{1-31-66}$$

165

$$\frac{WW}{2\text{-}10\text{-}66}$$
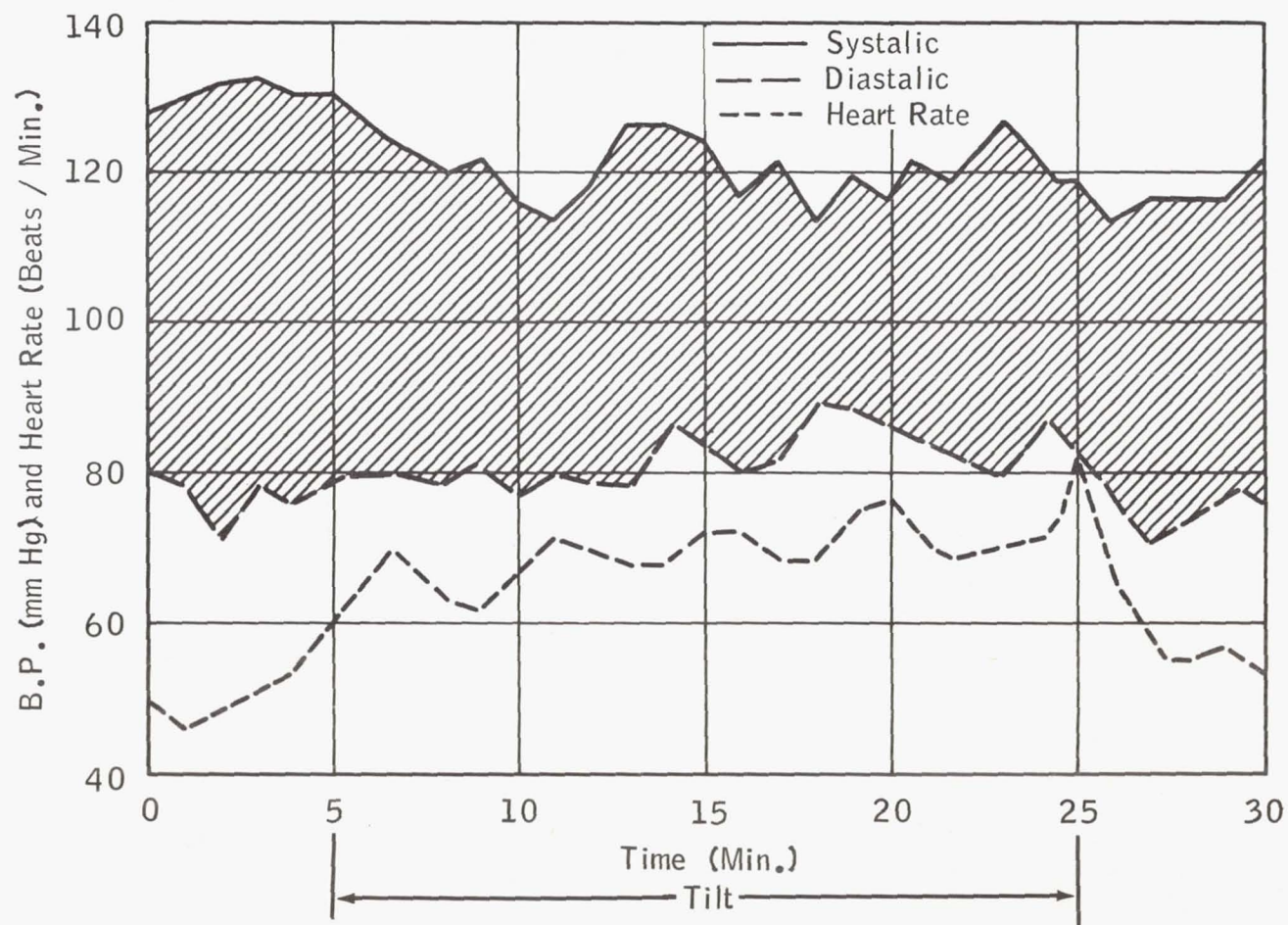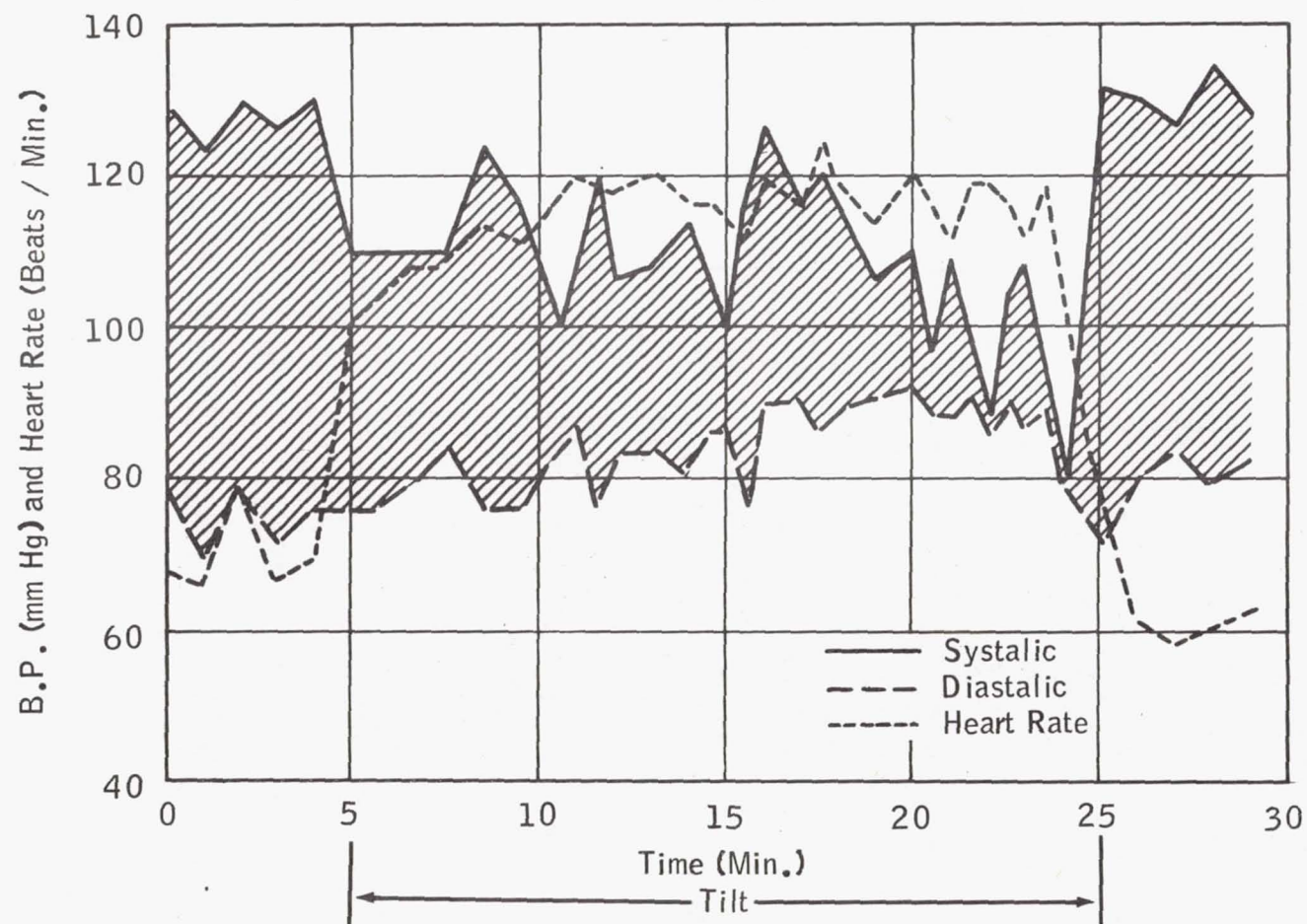
THE ROLE OF 9-α-FLUOROHYDROCORTISONE AS A COUNTER-

MEASURE TO POSTRECUMBENCY ORTHOSTATISM

William M. Smith, M.D., Kenneth H. Hyatt, M.D.
and Leonid G. Kamenetsky, M.D.
U. S. Public Health Service Hospital
San Francisco, California

Weightlessness or its analogues deprive man of the stimulating effects of hydrostatic pressure on the vascular system. As a result, normal postural cardiovascular reflexes become deconditioned. Additionally, blood volume is said to diminish due to inhibition of antidiuretic hormone and aldosterone by stimulation of volume receptors. These changes result in orthostatic intolerance on re-exposure to the effects of gravity. In some subjects, the orthostatic intolerance is severe enough to result in vasodepressor syncope with the attendant hazards of brain damage or death if the upright posture is not immediately terminated.

The use of cuff tourniquets to maintain vascular tone and prevent activation of the volume receptors has been shown to prevent cardiovascular deconditioning. The method has the disadvantage of requiring additional instrumentation and an adequate gas supply during inflight use. Antigravity suits, which have been successful in cases of idiopathic orthostatic hypotension should also obviate the effects of cardiovascular deconditioning. Again, this would require that the space suit be made even more complex and cumbersome.

Certain similarities between the manifestations of cardiovascular deconditioning and idiopathic orthostatic hypertension, plus the excellent therapeutic results obtained with 9-α-fluorohydrocortisone in the latter, suggested that this drug might be of value in the prevention of the orthostatic intolerance of weightlessness. A dosage was selected for use in our bedrest simulated weightlessness study which would result in sodium and water retention and plasma volume expansion, but which hopefully would not result in recumbent hypertension. This dosage was 0.1 mgm twice daily, and in these studies was not associated with elevations of resting blood pressure.

MATERIAL AND METHODS

The data to be reported is derived from 12 normal male volunteers from the Federal Correctional Institution, Lompoc, California. Ages ranged from 24 to 30 years. All subjects successfully tolerated a 20-minute 70° passive tilt prior to entry into the study. This tilt was performed without vascular instrumentation.

All subjects were placed on a controlled metabolic formula diet 48 hours prior to initiating the study. They were maintained on this diet during a 7-day ambulatory phase and a 14-day bedrest phase. Six subjects received 0.2 mgm of 9-α-fluorohydrocortisone daily during the bedrest phase. All excretions were collected during both phases. Urine was analyzed for electrolyte content, creatinine, nitrogen, 17-hydroxycorticosteroids, aldosterone and catecholamines. Stool analyses are pending. Blood volume was measured at regular intervals by the RISA method, using 10-, 20-, and 30-minute sampling with zero extrapolation. At the end of each phase, pulmonary artery catheterization and brachial artery cannulization were performed. Brachial and pulmonary artery pressures were measured with Statham P23D transducers. Cardiac output, mean circulation time and central blood volume were determined by injection of indocyanine green into the main pulmonary artery and constant withdrawal of blood from the brachial artery through a cuvette densitometer. Heart rate was recorded beat-by-beat by an ECG coupled R-R interval tachometer. Respiration was recorded by an impedance pneumograph. Resting supine studies were obtained, and subjects were then placed in a 70° passive tilt with continuous recording of heart rate, ECG, brachial and pulmonary artery pressure and respiration. Transducers were zeroed at the phlebostatic axis for both supine and tilt positions. Cardiac output determinations were performed at 5 and 18 minutes, and in some cases at 10 minutes of tilt. After recovery from tilting, hemodynamic response to 50W steady-state supine bicycle exercise was measured. The catheterization procedure was terminated after the measurement of hemodynamic response to injection of 3.0 mgm tyramine. Plasma and urine were collected for study of catecholamine response to tyramine. In addition to hemodynamic studies, oxygen consumption and minute ventilation were measured at rest, and during steady-state exercise.

Pressure and heart rate data to be presented were determined each minute by average data during two representative respiratory cycles.

RESULTS

The duration of tolerance of the 70° passive tilt for the individual subjects is shown in table I. We were disappointed, but not surprised, to find that less than half of the subjects were able to tolerate the prerecumbency study after vascular instrumentation had been performed. Since the situation after bedrest is identical and is the same for both control and treated groups, comparative results are considered valid. Table I illustrates the distinct improvement in postrecumbency tilt tolerance in the 9-α-fluorohydrocortisone group. In this group, only five subjects were studied postrecumbency. The sixth subject developed persistent atrial fibrillation during the postrecumbency catheterization and the study was cancelled.

TABLE I.- 70° TILT TOLERANCE

	Control group				9-α-fluorohydrocortisone group				
Subject	Before bedrest		After bedrest		Subject	Before bedrest		After bedrest	
	Min	Sec	Min	Sec		Min	Sec	Min	Sec
1	13	0	18	10	3	9	24	20	0
2	9	45	12	20	5	10	30	20	0
4	20	0	2	30	7	20	0	20	0
6	20	0	19	30	9	12	30	20	0
8	20	0	20	0	11	15	15	11	30
10	8	30	20	0	A	17	20	--	--

The one known postrecumbency failure in the treated group developed long runs of supraventricular and ventricular tachycardia during catheter manipulation postrecumbency. These stopped when the catheter was removed to the high right atrial position. The study was completed although the subject complained of epigastric fullness in association with the arrhythmias.

Figure 1 shows the classic deconditioning response with complete tolerance of the tilt test prerecumbency and marked orthostatic intolerance postrecumbency. Prerecumbency, the cardiac output, stroke volume and central blood volume remained relatively stable after the initial orthostatic drop. Syncope occurred before studies were performed postrecumbency. This case was in the control group.

Figure 2 reveals the factor of individual variation of response to recumbency in nontreated subjects. This man developed vasodepressor syncope prerecumbency. His period of bedrest was 19 days rather than the usual 14, due to a brief febrile illness; yet he was able to tolerate the full tilt procedure postrecumbency. Only one other subject from the control group tolerated the postrecumbency tilt. In that case, the subject had also tolerated the prerecumbency tilt.

Figure 3 is representative of the 9-α-fluorohydrocortisone-treated subjects. Tilt intolerance was present before bedrest and drug therapy, and after these measures, there was a stable tilt response. This subject actually augmented his cardiac output early in the tilt. This was associated with a marked rise in blood pressure.

Figure 4 is also representative of the treated group. In this case, both tilt procedures were tolerated.

Figure 5 shows the hemodynamic data of the treatment failure subject. In this case, pressure fall postrecumbency was progressive, but the commonly seen fall in heart rate did not occur. The only complaint of the subject was mild nausea. In view of the marked pressure drop, it was deemed unwise to await further developments, and the tilt was terminated.

Table II shows the composite results for the control and treated groups with regard to central blood volume, cardiac index, stroke index, and heart rate at 5 minutes of tilt. The time was chosen for comparison because results were available on all subjects except the one who developed vasodepressor syncope at 2-1/2 minutes postrecumbency.

Tilting resulted in an approximate 15-percent decrease in central blood volume in both groups before bedrest. After bedrest, the decrease became greater in the control group and less in the treated group. The fall in cardiac index was approximately the same in both groups at prerecumbency. While the fall increased in the control group postrecumbency, the treated group again showed a lesser drop.

Figure 1. - Response of deconditioning.

Subject no. 4

Before Bedrest

END TILT

After Bedrest

?

?

?

END TILT

REST

DURATION OF 70° TILT (minutes)

DURATION OF
50 WATT
HORIZONTAL
EXERCISE (min.)

——— CARDIAC OUTPUT (liters/minute)
·············· CENTRAL BLOOD VOLUME (liters)
–·–·–· STROKE VOLUME · 10^{-1} (ml.)
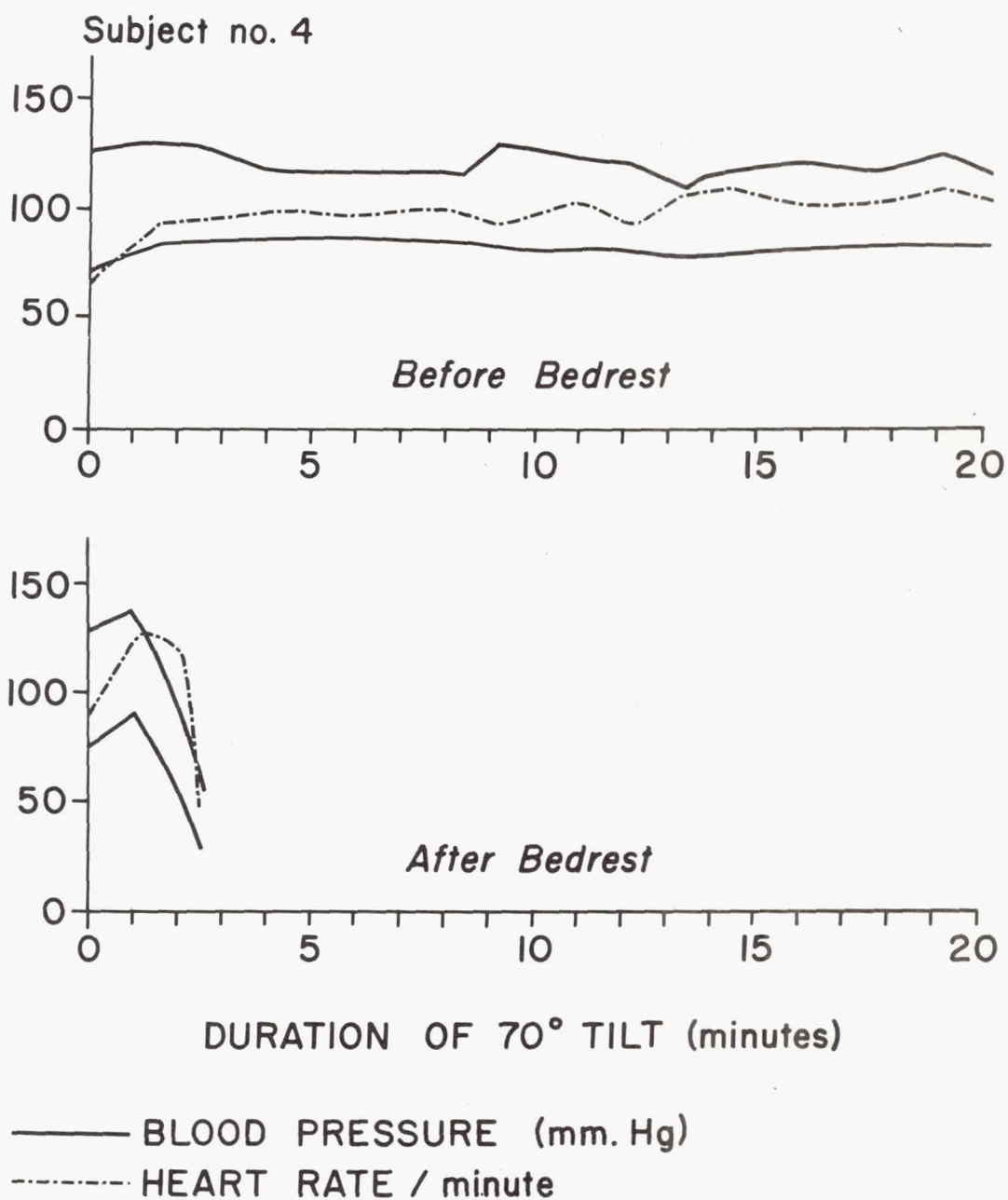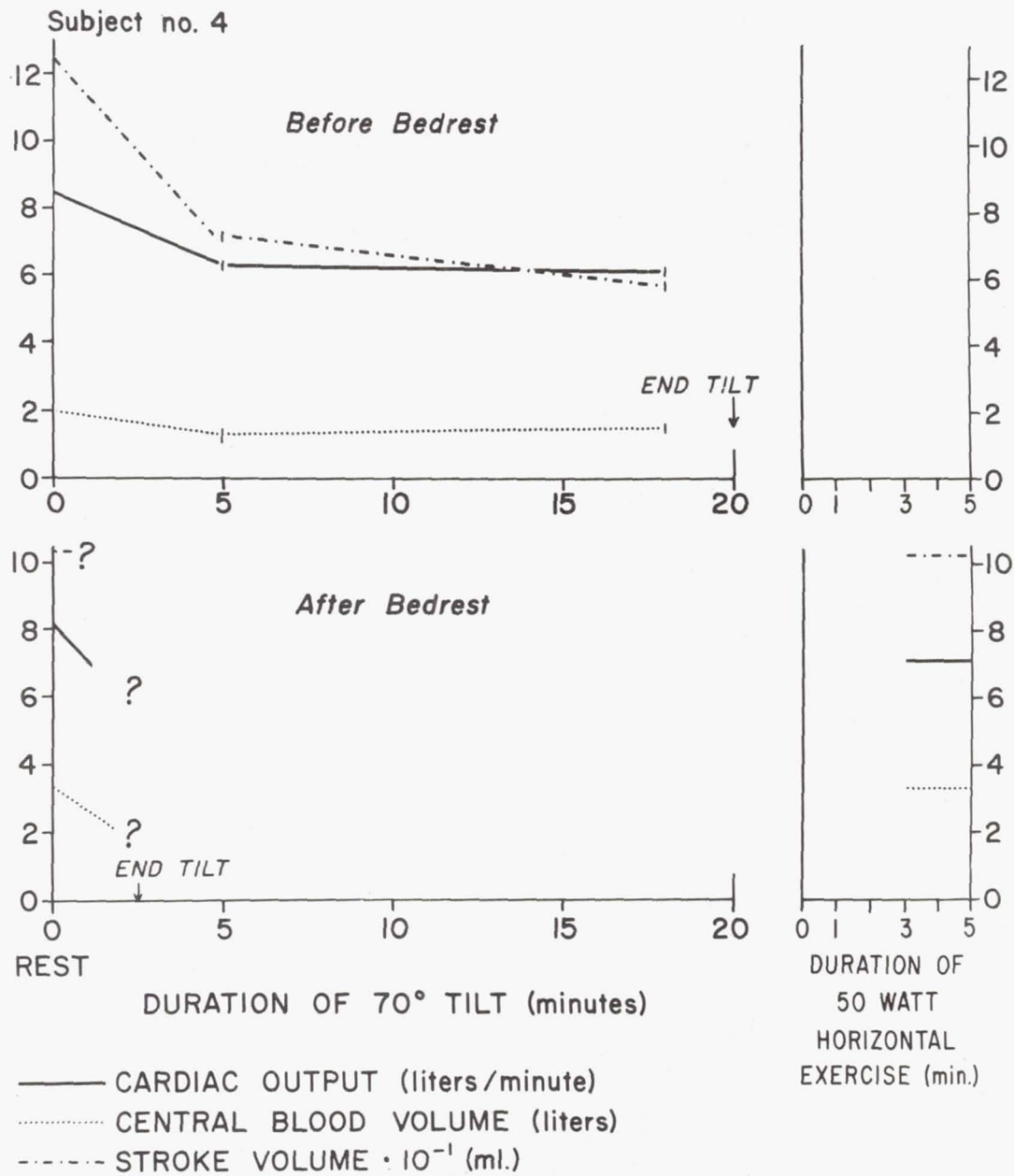
Figure 1. - Response of deconditioning - concluded.
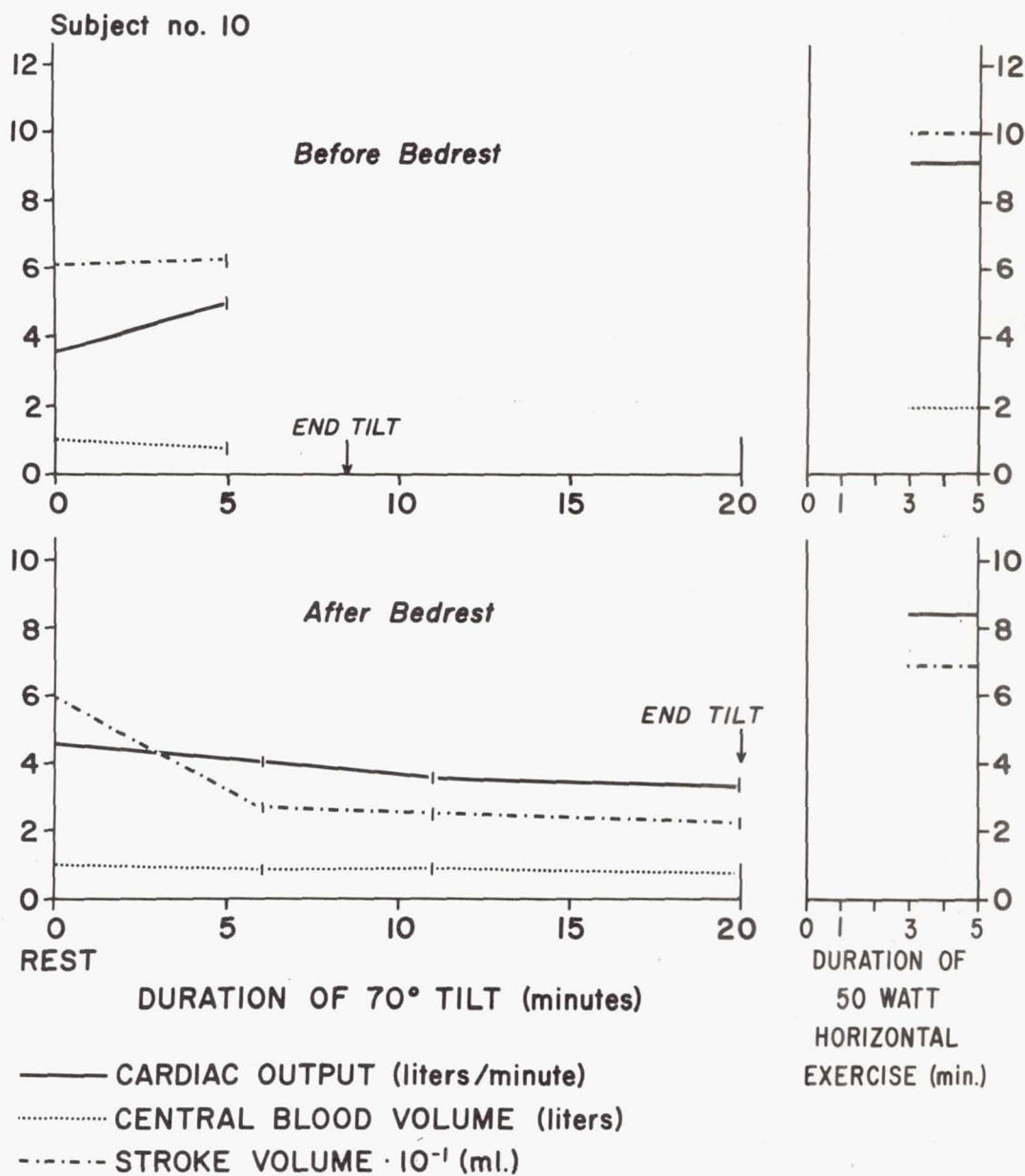
Figure 2. - Factor of individual variation of response to recumbency in non-treated subjects.
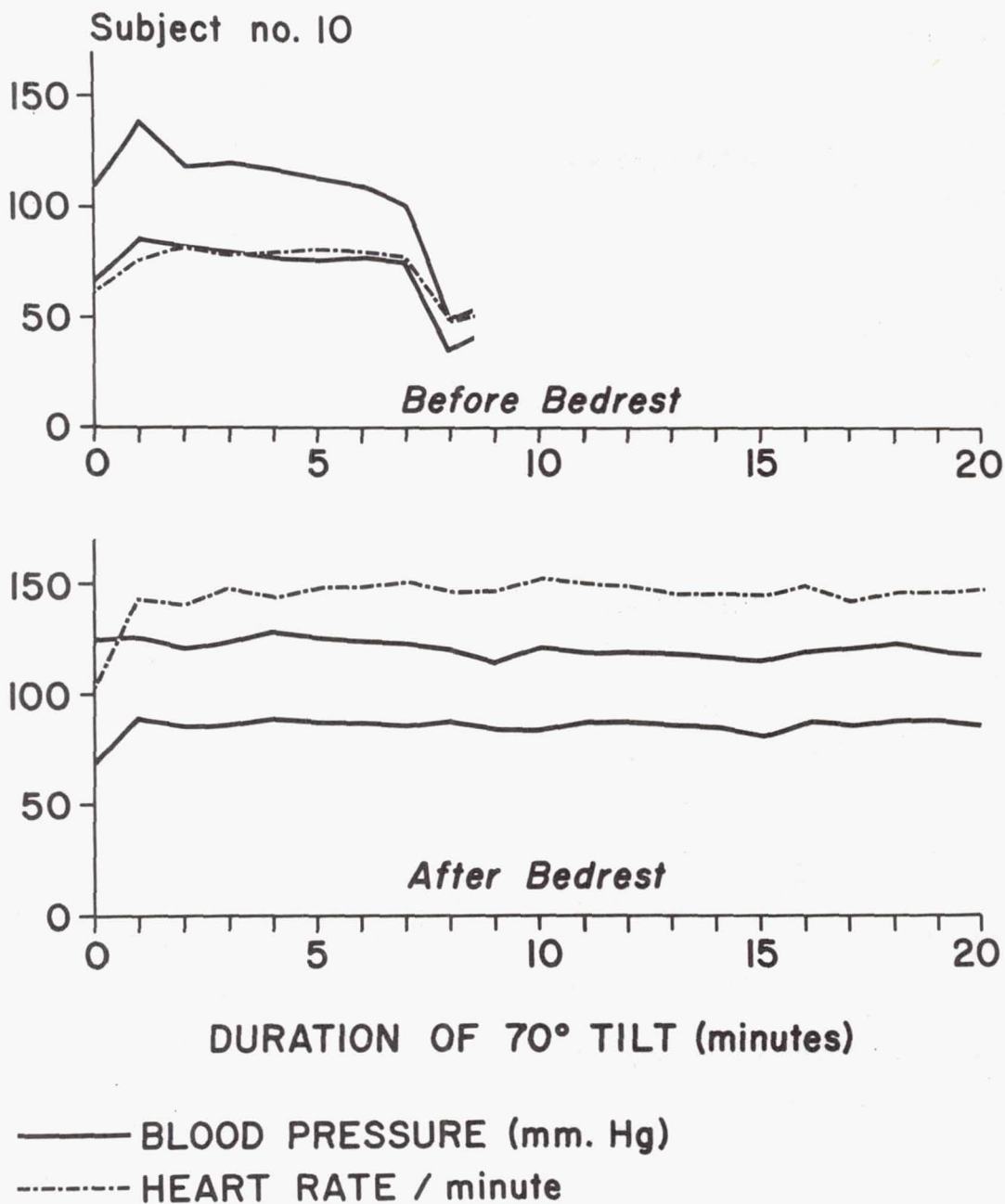
Figure 2. - Factor of individual variation of response to recumbency
in non-treated subjects - concluded.
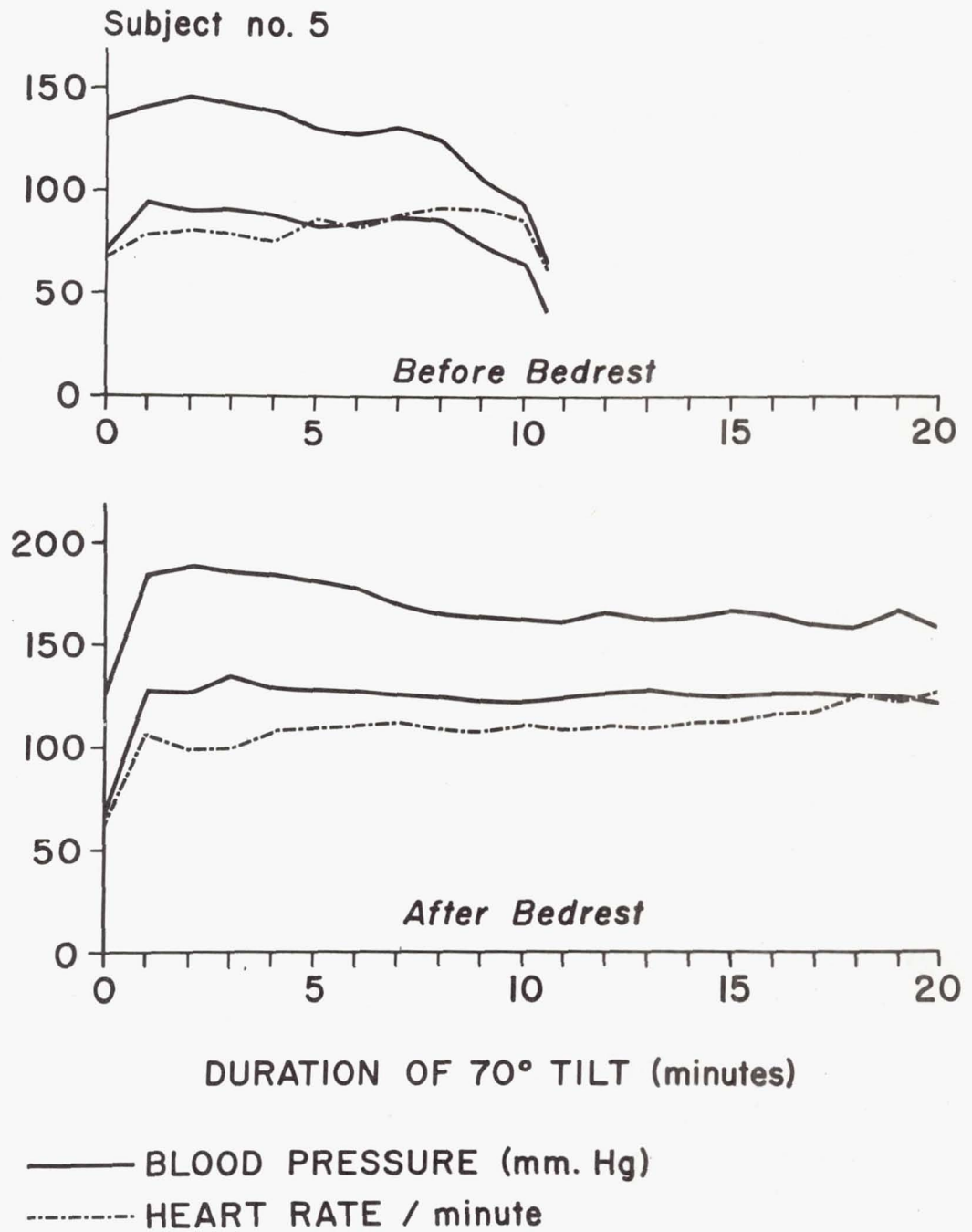
Figure 3. - Graphs are representative of the 9-α-fluorohydrocortisone-treated subjects.
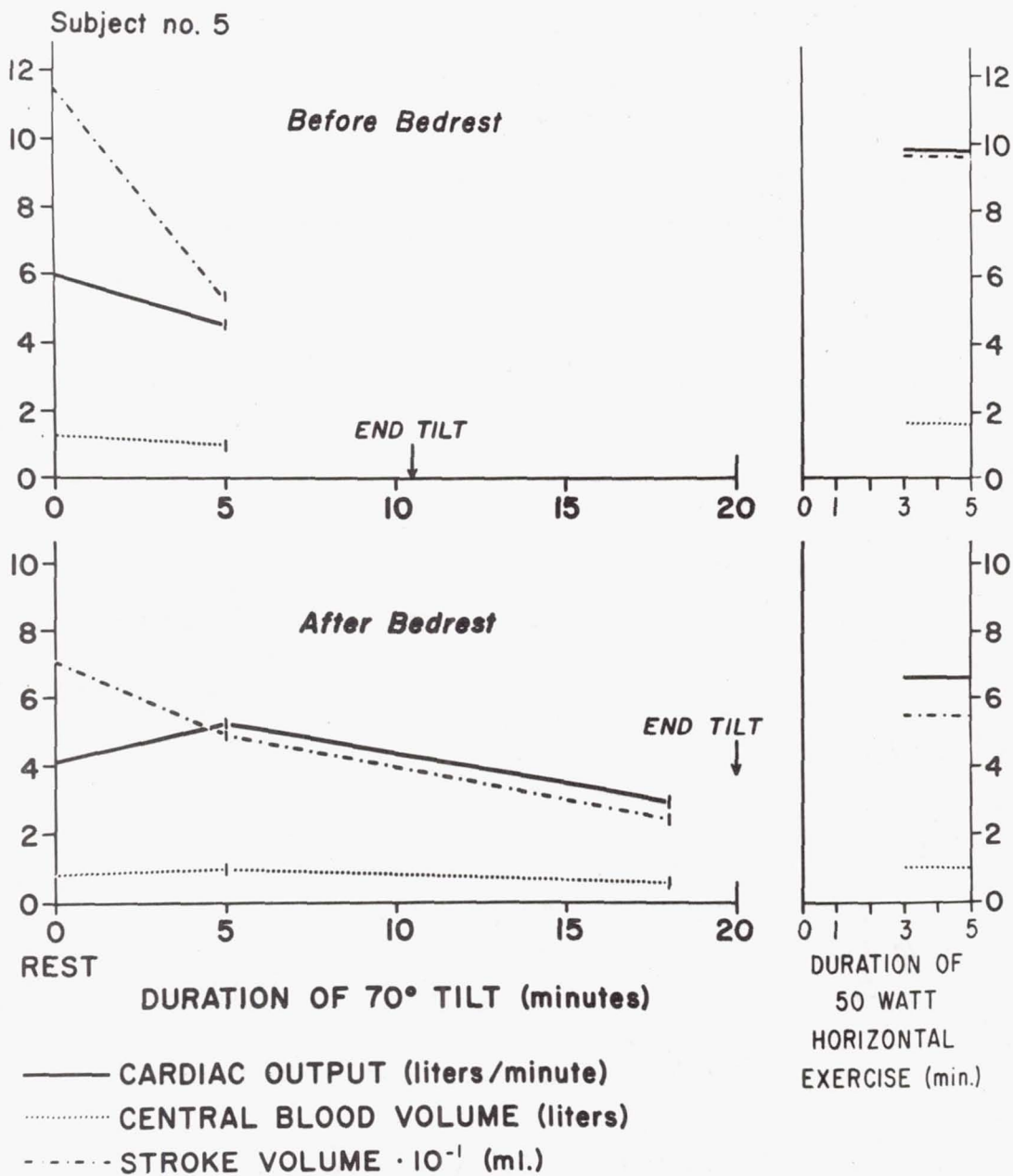
Figure 3. - Graphs are representative of the 9-α-fluorohydrocortisone-treated subjects - concluded.

Figure 4. - Graphs are representative of the 9-α-fluorohydrocortisone-treated groups.

178
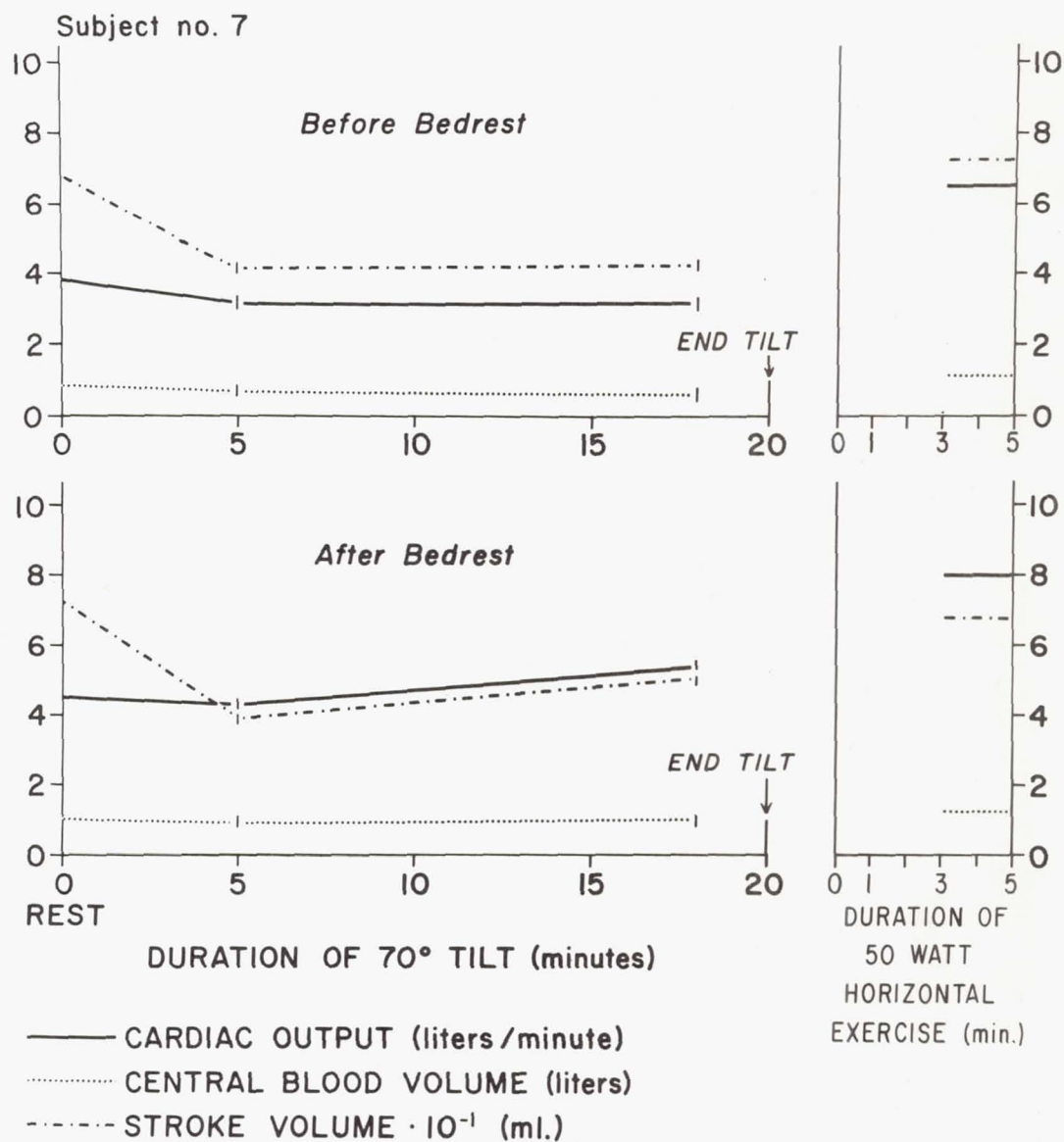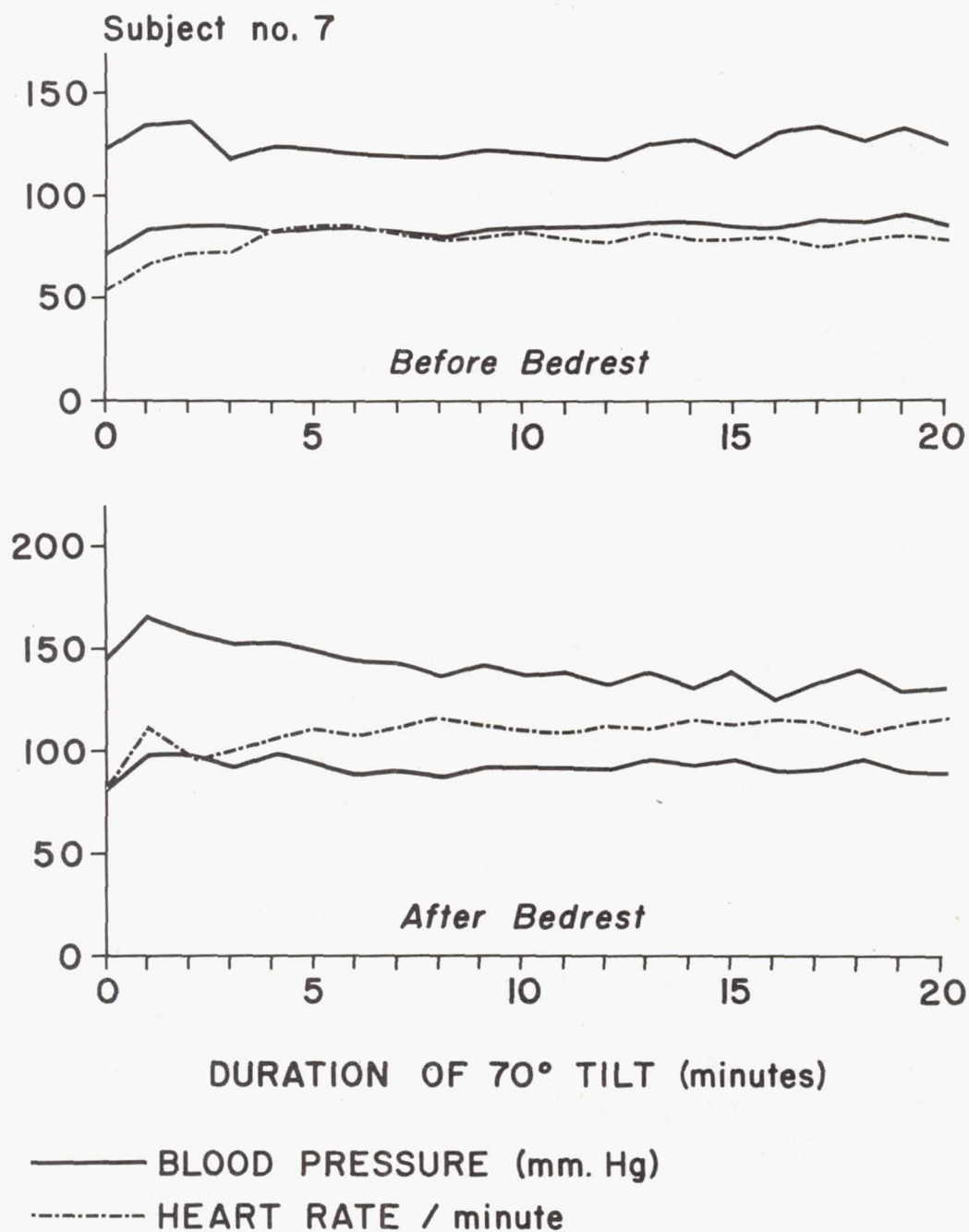
Figure 4. - Graphs are representative of the 9-α-fluorohydrocortisone-treated groups - concluded.
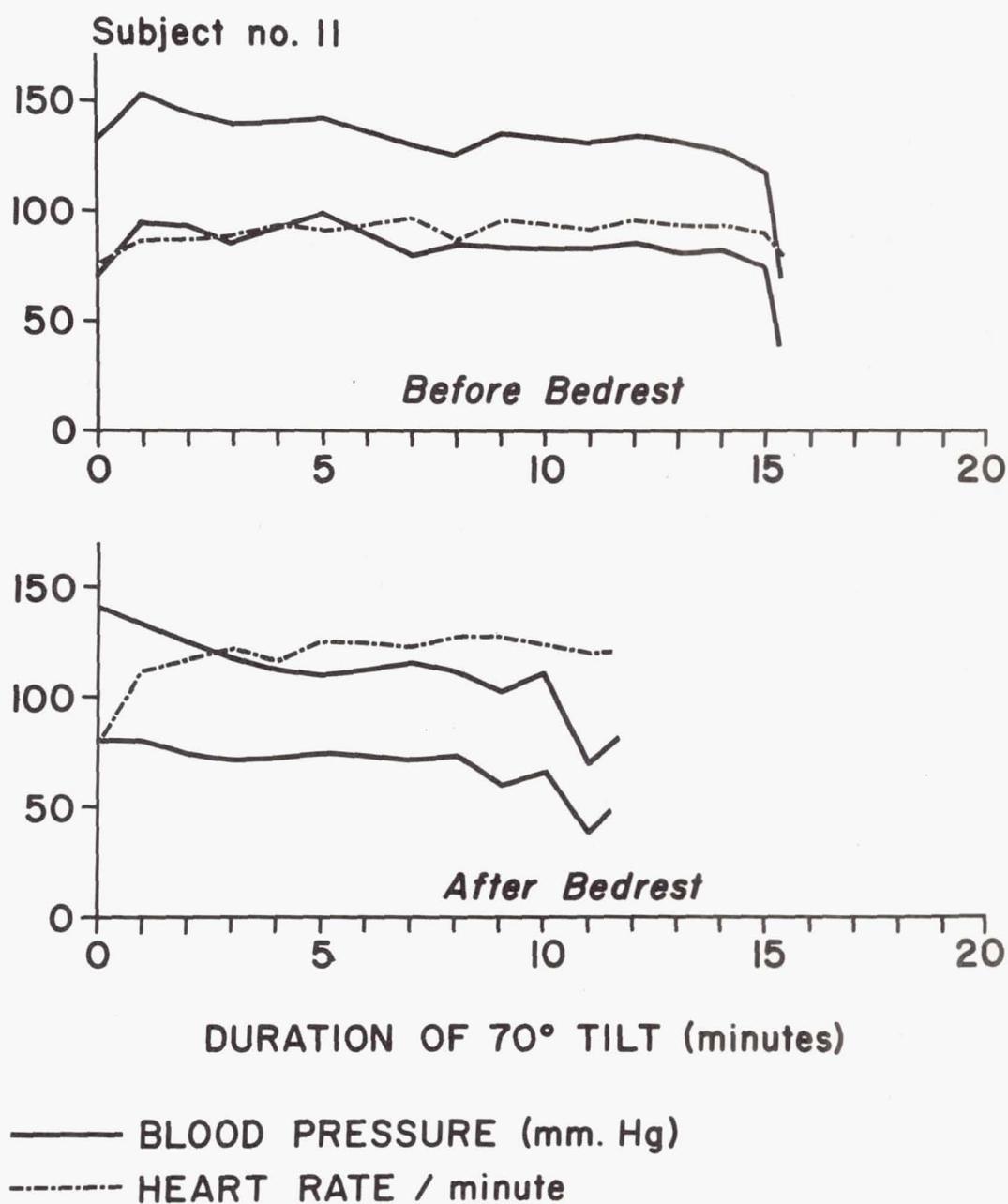
Figure 5. - Hemodynamic data of the treatment failure subject.
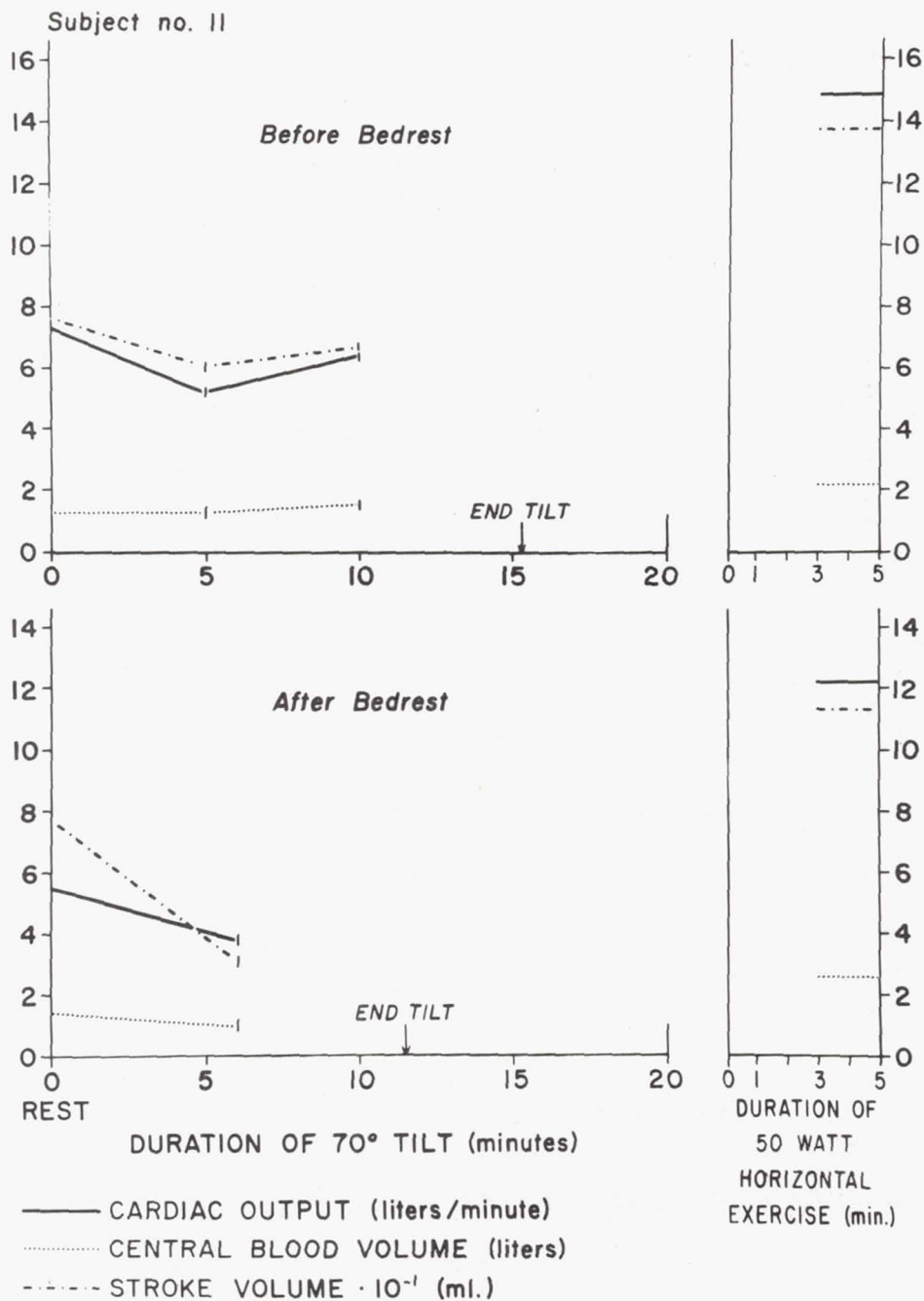
Figure 5. - Hemodynamic data of the treatment failure subject - concluded.

TABLE II.- ALTERATIONS PRODUCED BY 5 MINUTES OF 70° TILT

		Central blood volume, ml			Cardiac index, $L/min/M^2$			Stroke index, ml/M^2			Heart rate		
		Mean	Percent change	Difference, percent	Mean	Percent change	Difference, percent	Mean	Percent change	Difference, percent	Mean	Percent change	Difference, percent
Before	rest	1131			3.19			39.2			71		
	tilt	947	-16.3		2.79	-12.5		30.4	-22		97	+36	
Control				-4.9			-11.6			-27			+16
After	rest	1211			3.45			39.8			87		
	tilt	954	-21.2		2.62	-24.1		20.0	-49		133	+52	
Before	rest	1109			2.85			45.2			63		
	tilt	937	-15.5		2.41	-15.4		26.6	-41		95	+50	
9-Alpha				+5.4			+3.0			-6			+15
After	rest	1089			2.73			40.0			73		
	tilt	951	-10.1		2.39	-12.4		21.0	-47		121	+65	

The treated group would appear to be less stable prerecumbency than the untreated group in that heart rate increase was greater with a resultant larger magnitude fall in stroke volume and, in fact, this was the case. In the early phases of the study, subjects who did poorly on the initial tilt were selected for drug treatment, this effectively loading the 9-α-fluorohydrocortisone group with unfavorable subjects.

Postrecumbency, the resting heart rates of the treated groups were lower than those of the control group. They remained lower after 5 minutes of tilt although the change from the resting level was greater than in the control group. Absolute stroke index in the two groups was approximately the same, with the treated group showing a smaller relative change when compared with prerecumbency results. This is more apparent than real because of the large magnitude change in prerecumbency stroke index in the treated group.

Figure 6 shows blood volume and balance data on the typical and atypical control subjects. The accumulative sodium balance was determined by subtracting output from intake and further allowing 10 meq/day for extrarenal sodium loss. Sodium loss was profound during bedrest. In both cases, there is a drop in blood volume early in bedrest. In the subject remaining recumbent for 19 days, blood volume had returned to prebedrest levels at the end of the period of recumbency.

Figure 7 reveals similar data for the typical 9-α-fluorohydrocortisone-treated subjects. Note the later onset of natruresis as well as the overall diminution of sodium loss. Also noteworthy is the absence of plasma volume decrement during recumbency.

Figure 8 shows data for the 9-α-fluorohydrocortisone failure case. Sodium loss is not as remarkable as in the control group. In this case, there was a plasma volume decrease which persisted throughout bedrest.

The average total sodium loss for the control group was 342 meq whereas the average loss in the treated group was 240 meq. This was significant at the 0.05 level ($P < 0.05$).

Figure 9 is a composite of all plasma volumes done on subjects in each group during the indicated periods. The bars represent 95 percent confidence limits. There was a significant drop in plasma volume during early bedrest in the control group. This returned toward control levels late in the bedrest period. No significant changes in plasma volume occurred in the 9-α-fluorohydrocortisone group.
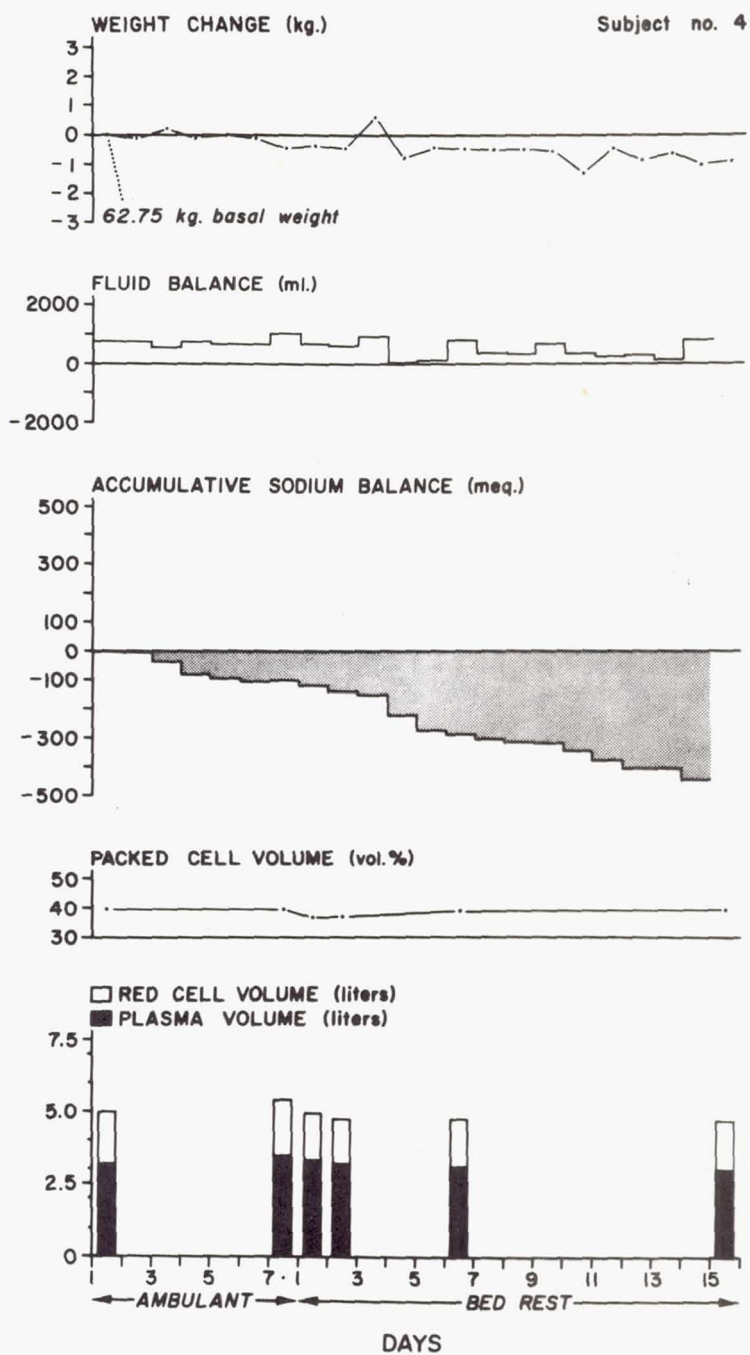
Figure 6. - Blood volume and balance data on the typical and antypical control subjects.
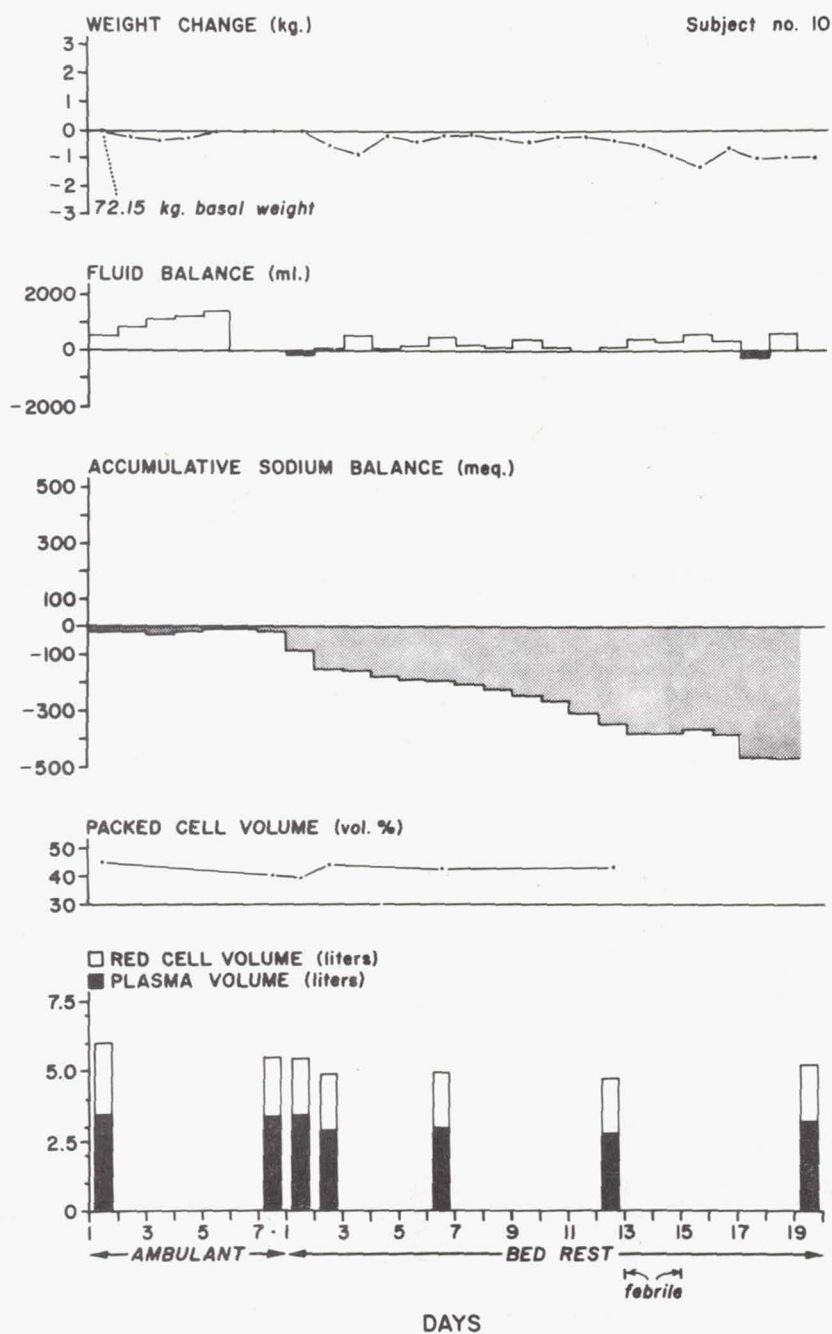
Figure 6. - Blood volume and balance data on the typical and antypical control subjects - concluded.
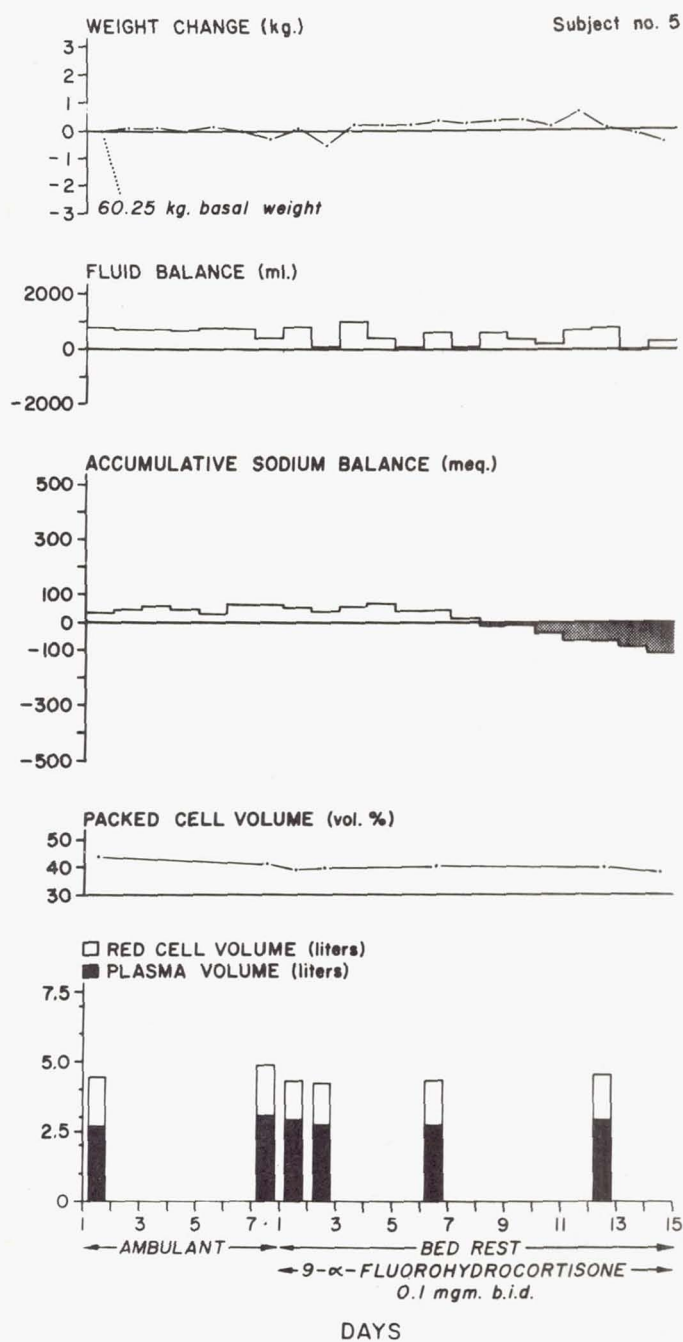
Figure 7. - Data for the typical 9-α-fluorohydrocortisone-treated subjects.
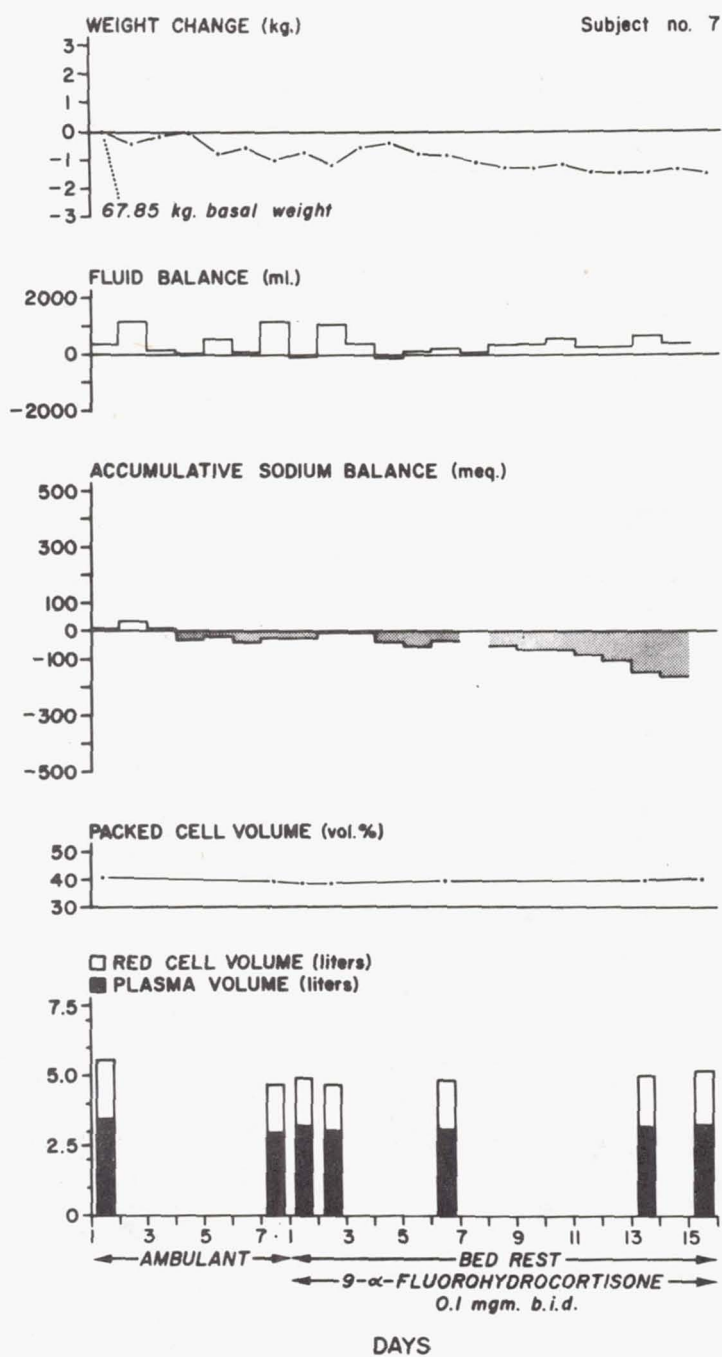
Figure 7. - Data for the typical 9-α-fluorohydrocortisone-treated subjects - concluded.
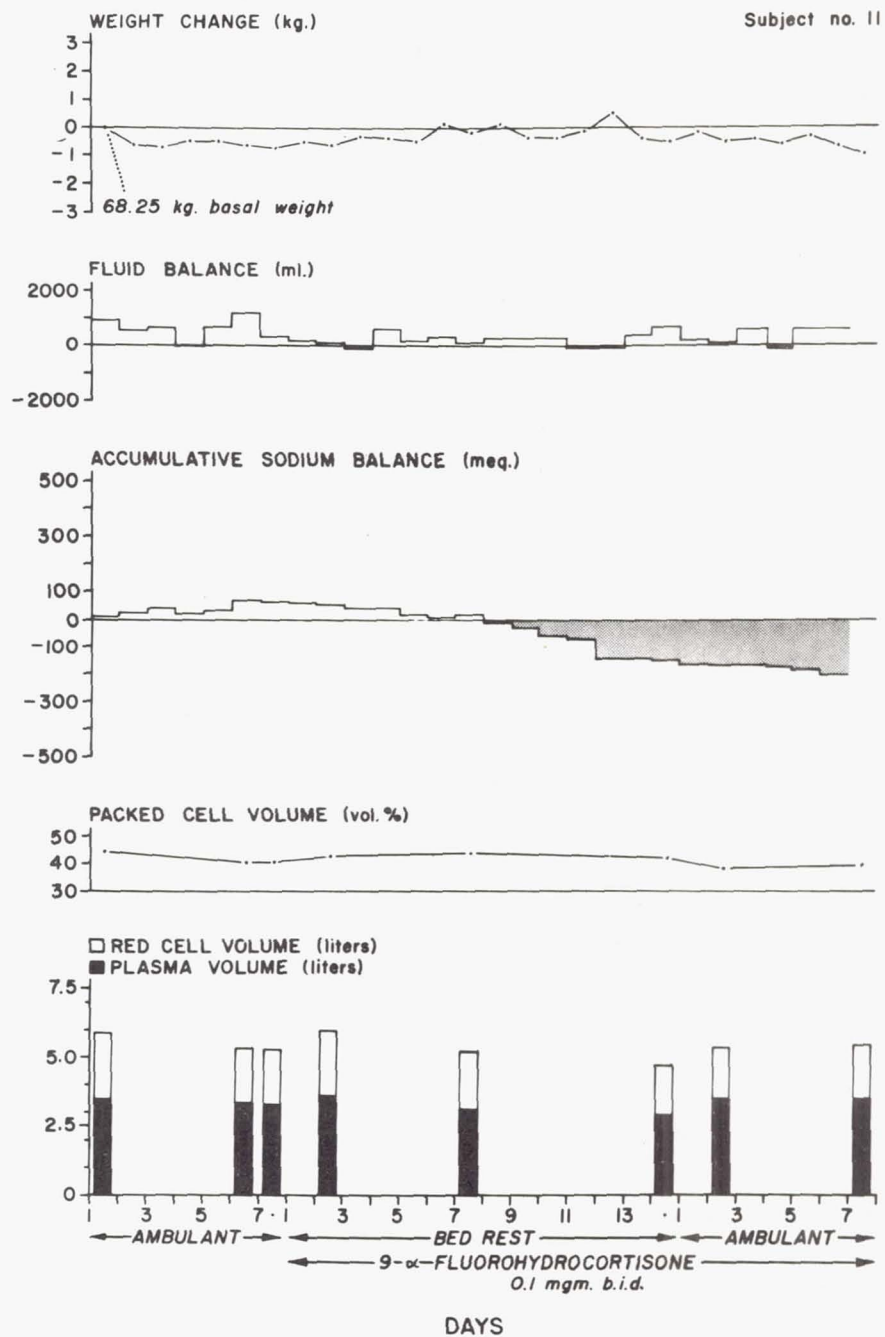
Figure 8. - Data for the 9-α-fluorohydrocortisone failure case.

PLASMA VOLUME
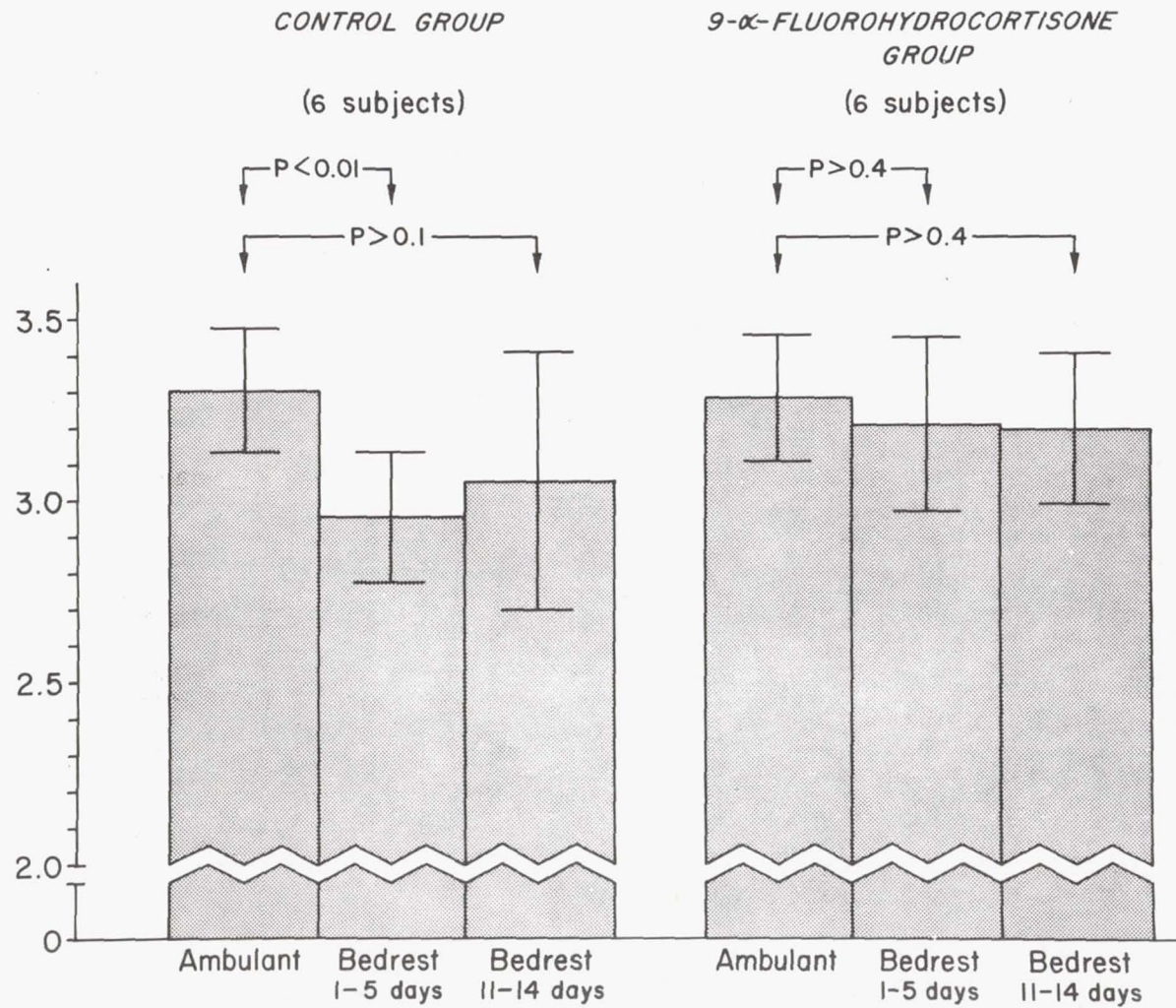
Figure 9. - Composite of all plasma volumes done on subjects in each group.

Figure 10 illustrates the response to tyramine injection in the two groups before and after bedrest. The notable difference is the diminished response to tyramine after two weeks therapy with 9-α-fluorohydrocortisone.

Originally, it had been planned to have the subjects void immediately before tyramine injection and at hourly intervals for 2 hours after tyramine. Due to the stress of tilting and exercise, only a few subjects were able to void before tyramine. It will therefore not be possible to assess the catecholamine excretion resulting solely from the tyramine injection.

Analysis of the urinary catecholamine composite response to tilting, exercise, and tyramine is incomplete and will not be presented, but a preliminary look suggests a decreased postrecumbency excretion in the majority of control subjects, and variable results in the treated group.

DISCUSSION

To date, our results indicate that any subject placed at prolonged bedrest develops cardiovascular deconditioning. This is manifested by a larger drop in central blood volume during 70° tilt after bedrest. This most likely results from greater pooling of blood in the capacitance vessels. Diminished central blood volume results in a reduced cardiac output. Baro-receptors in the aortic arch and carotid sinus are stimulated with a resultant increase in peripheral vascular resistance and heart rate. The great increase in heart rate during postrecumbency tilting is the most striking change seen. In most cases, vasodepressor syncope occurs during passive tilting. At this time, marked vagotonia replaces the initial adrenergic effects. The trigger mechanism for vasodepressor syncope is not readily apparent unless, as Sharpey-Shafter has suggested, the increased emptying of the ventricles activates the reflex. It is also possible that greater pooling of blood in the viscera may be the necessary ingredient. The postulate of a sudden rise in carotid sinus pressure producing a vagal overshoot would not apply in the present study as no increase of pressure occurred immediately before the pressure drop. However, this would account for the cases of severe vasodepressor syncope seen when a Valsalva maneuver is performed during tilting.

Cardiovascular deconditioned subjects differ from those with idiopathic orthostatic hypertension in their manifestation of prompt cardio-acceleration and initial rise in diastolic and mean arterial

Figure 10. - Brachial artery systolic pressure response to tyramine.

Before Bedrest

After Bedrest

% RISE ABOVE RESTING PRESSURE

BASELINE — PEAK RESPONSE 30-90 SECONDS AFTER TYRAMINE

BRACHIAL ARTERY SYSTOLIC PRESSURE RESPONSE TO TYRAMINE

——— CONTROL GROUP

—·—·—·— 9-α-FLUOROHYDROCORTISONE GROUP
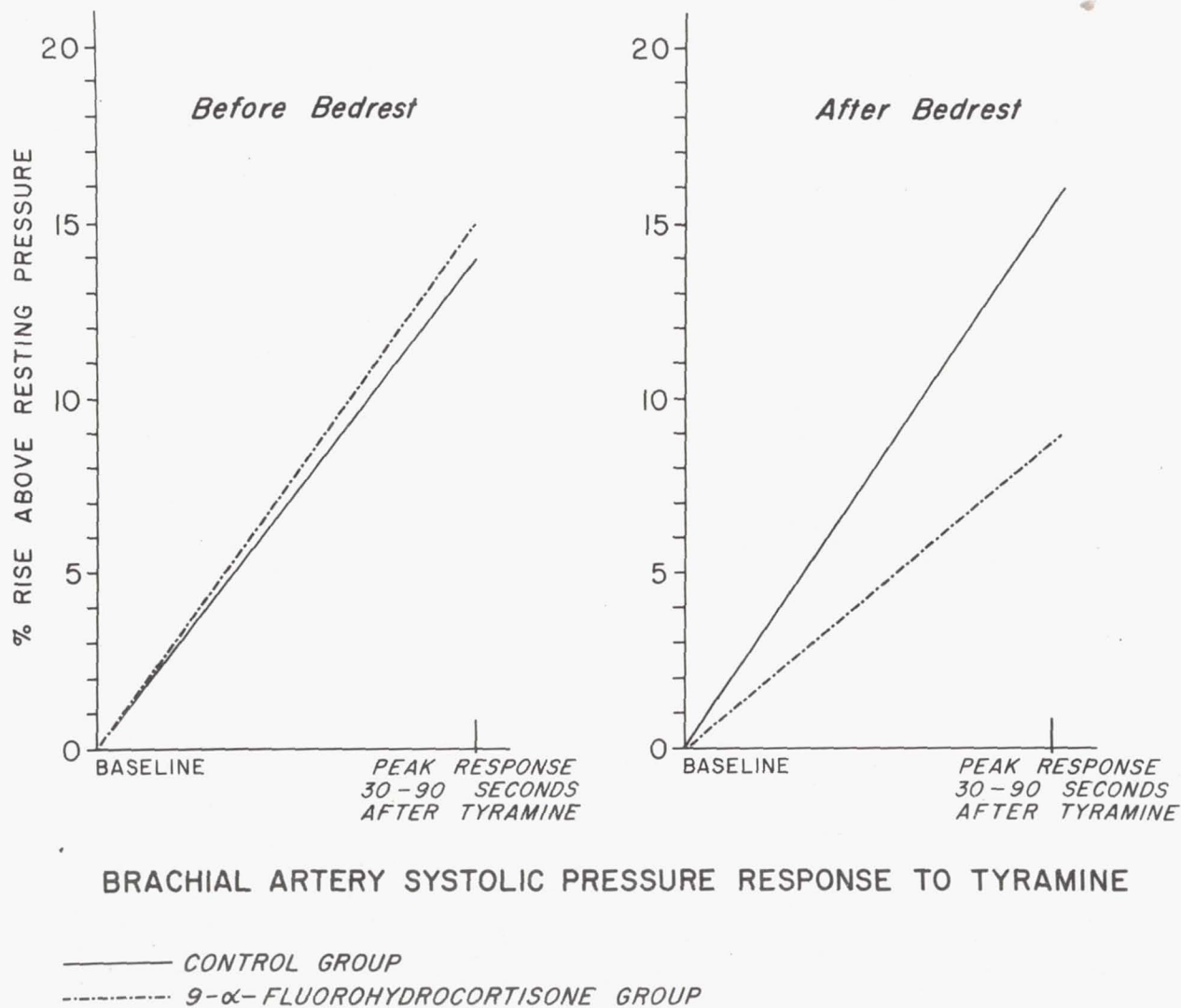
pressure. Furthermore, despite certain similarities in electrolyte and water handling, plasma volume changes, and orthostatic intolerance, it is not established that a state of adrenergic insufficiency exists in or accounts for postrecumbency deconditioning. The unaltered response to tyramine in the untreated subjects implies a normal relationship between the readily releasable norepinephrine stores and arteriolar effectors.

The possibility of an isolated defect in the responsiveness of capacitance vessels to gravitational stimuli has not been excluded. Such a defect could account for the increased extremity volumes seen in deconditioned subjects. A possible alternative is to postulate some degree of incompetency of the venous valves. This would impede venous return and distend the capacitance vessels.

Any diminution of plasma volume will further compromise the already reduced venous return and ventricular filling. However, results of the present study suggest that plasma volume changes are not of primary importance in cardiovascular deconditioning.

The use of 9-α-fluorohydrocortisone appears to be beneficial in preventing the occurrence of vasodepressor syncope in the subjects studied to date. Correlating with this effect are the failure of central blood volume and cardiac output to show as great a decrement on postrecumbency tilting in the treated group. In addition, sodium loss is impeded and no significant drop in plasma volume occurs. Postrecumbency cardiac acceleration still occurs in the treated group. The one failure out of five complete studies was associated with induced arrythmias at the time of catheterization, and we cannot exclude the possibility that this contributed to or was responsible for the failure. An additional possibility which would account for both the increased myocardial irritability and the failure to prevent hypotension is potassium depletion.

Seager demonstrated a pressor effect of potassium in a patient being treated with 9-α-fluorohydrocortisone for idiopathic orthostatic hypotension, and pointed out the presence of hypokalemic alkalosis in another patient who failed to respond to 9-α-fluorohydrocortisone. Studies on rats have also shown a pressor effect of potassium. In addition, it has been shown that the blood pressure of hypertensives can be lowered by restriction of potassium intake. Although not mentioned in our results, hypokalemia could have been a factor in our failure case. Serum potassium at the onset of the study was 3.85 meq/L. On the day of postrecumbency catheterization, serum potassium was 3.15 meq/L.

The mechanism by which 9-α-fluorohydrocortisone exerts its beneficial effect is not clear. Plasma volume was not expanded in our treated subjects but neither was it significantly reduced by bedrest. It is well known that 9-α-fluorohydrocortisone administration can sustain blood pressure in subjects with idiopathic orthostatic hypertension despite no sustained elevation of plasma volume. A potentiation of the effects of endogenous norepinephrine by 9-α-fluorohydrocortisone has been suggested as a possible mechanism of action. This suggestion was based on studies which showed norepinephrine potentiation to occur with desoxycorticosterone acetate and glucocorticoid therapy. However, this was not found to be true for 9-α-fluorohydrocortisone in a subsequent study. The fact that the postrecumbency injection of tyramine in our treated group produced a significantly smaller increase in systolic brachial artery pressure than had occurred before treatment suggests that either less norepinephrine was available for release by this means, or that sensitivity was decreased, but in either case this response to tyramine makes norepinephrine potentiation a doubtful thesis.

Tobian has reviewed data which show that water and electrolyte changes in vessel walls may alter vascular reactivity and lumen size. This may occur as a result of altered molecular kinetics of actomyosin or by an effect on the membrane potential of smooth muscle. It is also possible that passive narrowing of vessel lumens may result from waterlogging of smooth muscle cells. The lower levels of natruresis seen in our treated subjects would be consistent with a more physiologic level of sodium in the vascular wall.

In summary, we feel that preliminary studies indicate that 9-α-fluorohydrocortisone has potential value in the prevention of the serious effects of cardiovascular deconditioning. Larger numbers of subjects must be studied before conclusive data are available and optimum dose schedule determined. The role of potassium in the success or failure of therapy requires further investigation.

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THE EFFECT OF INTERMITTENT LEG-CUFF INFLATION AND INTERMITTENT EXERCISE

ON THE TILT TABLE RESPONSE AFTER TEN DAYS BED RECUMBENCY

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Studies of the tilt table response of normal individuals date back to the turn of the century. Abnormal responses have been noted in a variety of circumstances, but the condition of cardiovascular deconditioning has aroused interest in recent years in aerospace medicine. Cardiovascular deconditioning generally is described as an ill-defined syndrome characterized by deterioration of normal compensatory reflexes or mechanisms as a result of experimental conditions which simulate various aspects of weightlessness. Deconditioning experiments have included bedrest, chair rest, water immersion, and space flight.

The usual response, upon change of a normal subject from the horizontal to the vertical position, is an increase in heart rate, a slight increase in diastolic pressure, and a slight decrease in systolic pressure. Cardiovascular deconditioning usually is said to occur after some experimental circumstance that alters the usual compensatory responses resulting in more pronounced changes in heart rate, a more rapid decrease in blood pressure, and the ultimate occurrence of signs and symptoms of syncope or impending syncope. It should be noted, however, that progressive changes in heart rate and blood pressure resulting in syncope, usually of the vasovagal type, occur in a fair proportion of healthy young adult males.

Various theories have been proposed to explain the mechanism resulting in cardiovascular deconditioning, including decrease in blood volume, sluggish venomotor reflexes that result in pooling of blood, and loss of muscle tone because of physical inactivity associated with the deconditioning experiment.

Various techniques have been used during deconditioning experiments in an attempt to prevent the development of tilt table manifestations of deconditioning. The studies of Deitrick, Whedon, and Shorr showed some protective effect was derived from periodic rocking beds. Miller interpreted some protection from a combination of various treatments of

preconditioning, exercise, and head-up bed position. Vogt found no definite protective effect from the performance of periodic Flack procedures during bedrest. Vallbona found a suggestive protective effect from intermittent large doses of isometric exercise. White and his group interpreted the difference in tilt table response of two groups of subjects, one of which was subjected to periodic short-arm centrifugation, as evidence of its efficacy in reducing manifestations of cardiovascular deconditioning.

The equipment needed and the complexity of some of the techniques which must be applied to provide small amounts of protection make their usefulness somewhat limited in the manned space flight situation. Graveline found a rather remarkable protective effect using intermittently inflated pressure cuffs on the four extremities of subjects normally deconditioned by short-term immersion in water. Vogt confirmed this protective effect in water immersion experiments, and suggested that his results occurred primarily as a result of inflation of cuffs on the upper extremities. Also, Vogt and Johnson have presented evidence that the difference in response may be associated with an abnormal transfer of a protein-fluid-electrolyte complex out of the vascular system into the extravascular space to account for part of the observed changes of deconditioning.

The purpose of this study was to evaluate the potential protective effect of two techniques which could be adapted to manned space flight. Periodic use of a Bungie-cord exerciser, of the type used as a cardiovascular provocative test in Project Mercury, was selected as one method because physical inactivity with decrease in muscle tone has been incriminated by some investigators as a possible mechanism of deconditioning. The other technique was periodic inflation of leg cuffs on the lower extremities to determine if a protective effect could be found in the bedrest situation as is found with water immersion. Cuffs were applied only to the lower extremities to simulate the experimental inflight experiment M-1, which was planned by NASA for the manned Gemini space flights. A cuff inflation-deflation cycle of 5 minutes on and 10 minutes off was selected because it required less air for inflation, and previous venous catheterization studies by the author indicated that several minutes of cuff inflation were required to obtain a significant increase in venous pressure. At the time of experimental design, the hypothesis was that periodic inflation of leg cuffs would increase venous pressure and thus result in a decreased transfer of fluid from the extravascular space into the vascular system. Such a technique, also, would provide periodic stimulation of venous reflex mechanisms from the periodic increase in venous pressure and the consequent pooling of blood.

METHOD

Subjects

Eleven healthy young adult male subjects participated in three periods of 10 days bedrest conducted at the Texas Institute for Rehabilitation and Research during the summer of 1964. Subject characteristics are shown in table I. Subject A.P.K. participated in the first period of recumbency only and was replace by subject L.F.E. Subjects who actively and regularly participated in physically competitive sports were classified as athletes. The other subjects were designated non-athletes.

Calendar of Experimentation

The calendar of experimentation is shown on figure 1. The subjects were divided into two groups for convenience in testing; one group went into bedrest a day before the other group. Accordingly, the first group of subjects was ambulated 1 day earlier than the second group. During the first recumbency period half of the subjects performed periodic Bungie-cord exercises and the remainder of the subjects had cuffs periodically inflated on their lower extremities. During the second period of recumbency, the treatments were reversed for the two groups of subjects. Finally, during the third period of recumbency, all subjects went through a period of bedrest without any preventive or treatment measure to define the effect of the experimental condition of bedrest. A detailed presentation of the experimental protocol is presented elsewhere. (See refs. 4 and 14.)

Experimental Circumstance

The subjects were admitted to the Texas Institute for Rehabilitation and Research as patients for experimental studies. During a 94-day stay at the hospital, they were fed controlled diets, the salt content of which approximated 8 to 10 grams per day. Fluid intake was ad libitum. In the intervals between recumbency periods, the subjects were maintained on controlled diets and sleep schedules. In the daytime, they were encouraged to follow activity patterns similar to that followed prior to admission, except for the imposition of food and sleep control. During the periods of recumbency, the subjects were required to remain flat in bed and were allowd one pillow under their heads, were allowed to roll from side to side in bed, and were allowed to turn on their sides to feed themselves.

TABLE I

Subject Characteristics

Subject Initials	Hospital Number	Age (yrs.)	Weight* (kg.)	Height* (cm.)	BSA** (m.^{2})	Occupation
M.A.C.	70020	23	65.3	177.8	1.81	Student(NA)
L.F.E.****	70028	24	74.3	188.0	2.00	Student(A)
R.S.H.	70021	22	65.2	172.4	1.77	Student(A)
J.A.H.	70022	23	81.1	179.0	2.01	Student(NA)
B.E.H.	70019	21	69.8	177.8	1.88	Student(NA)
A.C.I.	70018	22	51.0	163.0	1.52	Student(A)
A.P.K.***	70023	24	59.4	174.0	1.72	Student(NA)
W.F.M.	70024	23	66.4	171.0	1.78	Student(NA)
C.E.R.	70025	25	80.6	192.4	2.11	Student(A)
G.S.R.	70026	26	65.6	177.8	1.83	Student(A)
R.R.T.	70027	22	78.2	172.4	1.92	Student(NA)

A   Athlete
NA   Non-athlete
*   At the beginning of the experiment
**   Dubois Body Surface Chart (prepared by Boothby and Sandiford)
***   Participated only in the first period of bedrest
**** Participated only in the second and third periods of bedrest

CALENDAR OF EXPERIMENTATION

	S	M	T	W	T	F	S	
JUNE		1	2	3	4	5	6	
	7	8	9	10	11	12	13	
	14	15	16	17	18	19	20	
	21	22	23	24	25	26	27	RECUMBENCY PERIOD NO. 1
	28	29	30	1	2	3	4	
JULY	5	6	7	8	9	10	11	
	12	13	14	15	16	17	18	
	19	20	21	22	23	24	25	
	26	27	28	29	30	31	1	RECUMBENCY PERIOD NO. 2
AUGUST	2	3	4	5	6	7	8	
	9	10	11	12	13	14	15	
	16	17	18	19	20	21	22	
	23	24	25	26	27	28	29	
	30	31	1	2	3	4	5	RECUMBENCY PERIOD NO. 3
SEPTEMBER	6	7	8	9	10	11	12	

Legend:
- TILT
- PRE-RECUMBENCY OBSERVATION
- RECUMBENCY PERIOD
- RECOVERY PERIOD

Figure 1.- Calendar of experimentation.

Cuff treatment was employed 24 hours a day, using 3.75-inch-wide cuffs applied to the upper part of the thigh and inflated to a pressure of 70 to 75 mm Hg. The cuff inflation-deflation cycle was 5 minutes on and 10 minutes off, with the cuff being fully inflated in 5 to 8 seconds. Starting at 8:00 a.m., Bungie-cord exercises were performed hourly for 10 treatment periods a day. The subject performed exercises in the horizontal position by placing his feet in a bracket at one end of the rubber Bungie-cord exerciser to provide a fixed point against which to pull. The subject kept his legs in a partially flexed position at this time to provide muscular exercise to the lower as well as the upper extremities. The extent or length of pull allowed for each exercise was determined for each subject prior to bedrest by selecting an exercise load which produced a moderate amount of cardioacceleration in response to the exercise. The exercise consisted of 120 pulls on a prescribed Bungie cord at a rate of one pull per second.

Tilt Table Studies

Tilt table studies were performed before and immediately after each period of recumbency. Electrocardiographic data were obtained continuously with a strip chart recorder and recorded on magnetic tape for storage and future analysis. Intra-arterial blood pressure measurements were obtained from the right brachial artery through a Cournand needle connected to a Statham pressure transducer. Other measurements were made, including forearm blood flow, venomotor tone, leg circumference changes, plasma volume changes, et cetera; but for simplicity, these measurements will not be considered here.

Five minutes of control data were obtained with the subject in the horizontal position after the subject was considered to be in a baseline condition for the particular test circumstance. A Flack maneuver then was performed and 5 minutes later the subject was tilted manually, taking approximately 3 to 5 seconds, to a 70° head-up tilt position. The subject was supported in the upright position by an English-saddle type support, with most of the body weight being borne by the ischeal tuberosites, thus providing a passive tilt. The subject was kept in the upright position for 20 minutes unless syncope or impending syncope occurred. After tilt down, an additional 5 minutes of control data were obtained, followed by a repeat Flack maneuver, and the collection of 5 minutes of additional data. A schematic of the tilt procedure is shown on figure 2 and on figure 3 a subject is shown on a table tilted to the 70° position.
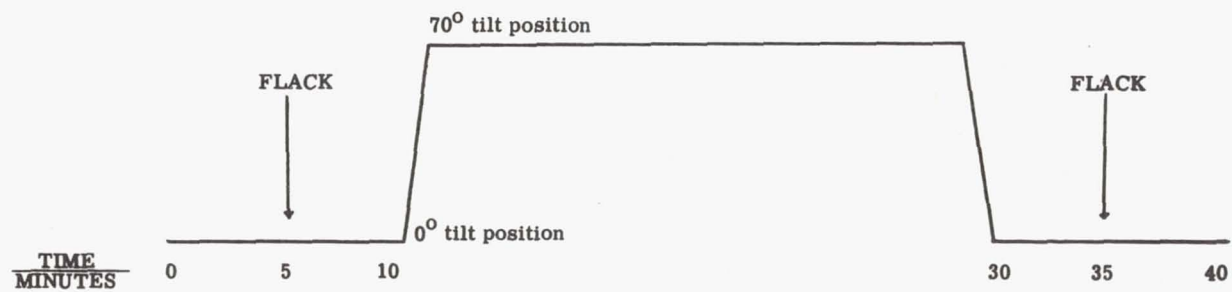
Figure 2. - Schematic of diagram of tilt procedure.
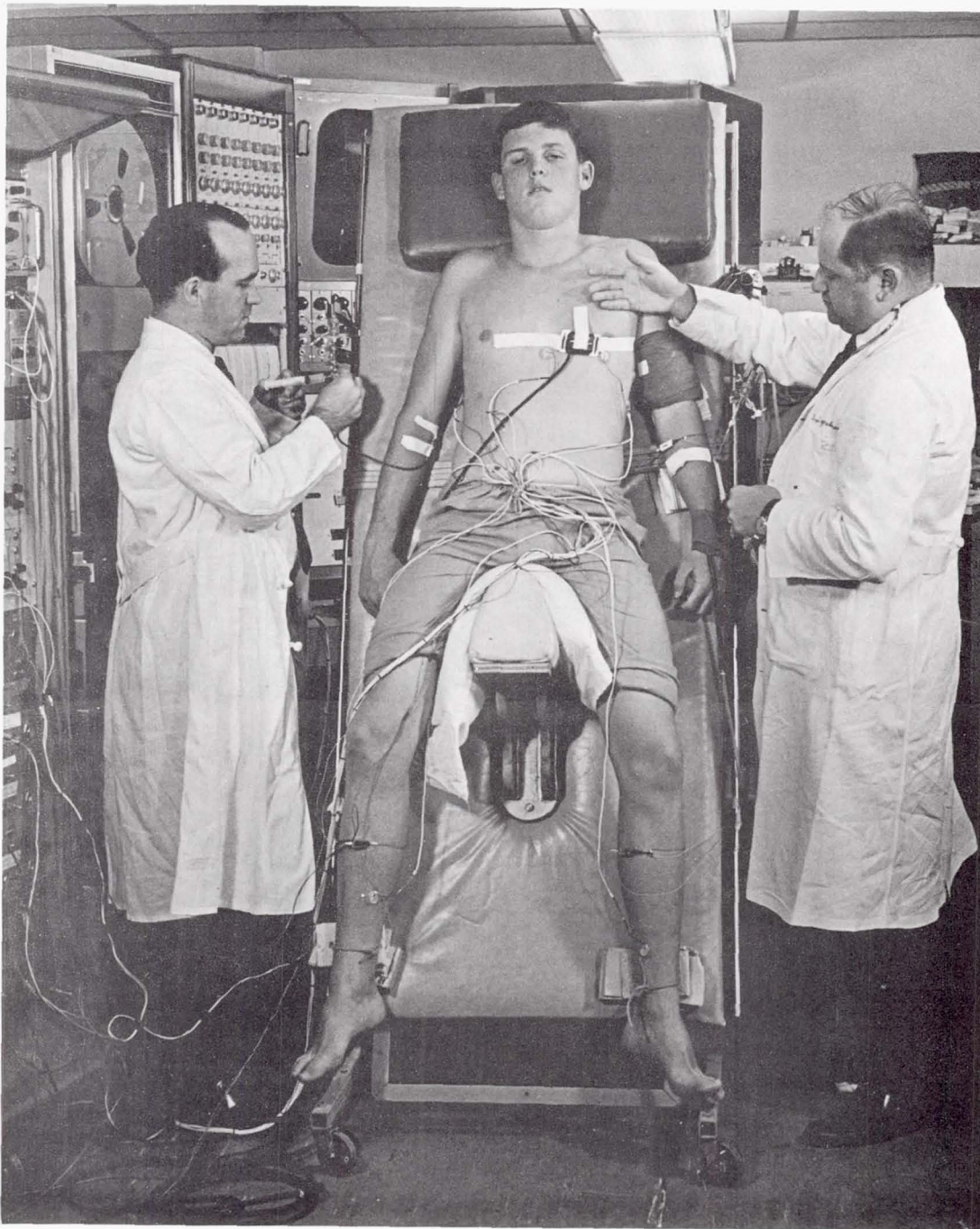
Figure 3. - Photograph of test subject in the 70° head-up tilt position.

Data Analysis

Heart rate and blood pressure data were analyzed by an objective approach described by Vogt. Heart rates were determined by counting the total heart beats in each successive minute during the tilt procedure. Blood pressure measurements were arbitrarily and systematically collected exactly at the beginning of each minute by reading the corresponding systolic and diastolic blood pressures. The pretilt control data is represented by the 5 minutes of data collected prior to the Flack test, and the posttilt data by the 5 minutes immediately following tilt down. For simplicity of discussion, the Flack maneuvers will not be considered in this paper.

From the heart rate and blood pressure information, a group of derived measurements were set up which would characterize the tilt response. An analysis of variance then was performed to select statistically significant changes which might characterize the effect of different treatments. The determination of analysis of variance utilized two main effects (treatment and nonathlete/athlete) and the interaction between the two to determine the residual term.

RESULTS

The results presented in this paper refer only to the studies conducted on the nine subjects who participated in all phases of the study. A summary is presented in table II of the F values and significance levels for the measurements selected to describe characteristics of the tilt table response from this experiment. The basis for selection of these measurements is described elsewhere. In the first column are the statistical comparisons of the tilts conducted prior to the three treatment periods. None of the measurements showed a change at a 5 percent significance level, indicating reproducibility in the tilt procedures conducted on different days. This also indicates that the 3-week interval between recumbency periods allowed recovery from the preceding cardiovascular deconditioning. In the second, third, and fourth columns the F values and levels of significance are shown for each measurement, after each treatment, compared with the measurements of the three pooled pretreatment tilt table procedures. The significant changes in a number of variables indicate that deconditioning occurred during all three treatment periods. In table III are presented the mean values for each measurement, thus indicating the magnitude and direction of change. In the fifth column in table II is presented a summary of the analysis of variance which compares the three posttreatment (during bedrest) tilts, indicating no statistically significant difference in the tilt procedures, except for the time to reach minimum pulse pressure.

TABLE II

Summary of F Values and Levels of Statistical Significance
of Measurements Derived from Tilt Table Procedures

Measurements	Pre Treatment Tilts	Pre vs. Post Bedrest	Pre vs. Post Cuffs	Pre vs. Post Exercise	Post Treatment Tilts
Time to tilt down	2.69NS	1.76NS	8.96**	5.00*	0.85NS
Avg HR pre-tilt	1.50NS	1.46NS	0.81NS	0.04NS	0.34NS
Max HR during tilt	1.46NS	23.29**	9.17**	19.39**	1.30NS
Min HR after tilt	0.46NS	3.65NS	3.98NS	2.01NS	0.03NS
Cng in HR with tilt	1.20NS	22.91**	7.81**	27.65**	2.39NS
Frac incr in HR	1.10NS	18.18**	6.71*	30.03**	1.81NS
Avg pre HR-avg post	0.53NS	1.12NS	0.87NS	4.18*	0.22NS
Time of max HR	0.53NS	0.00NS	3.27NS	0.65NS	1.04NS
Time to 0.8 max	0.50NS	0.14NS	2.54NS	0.93NS	0.67NS
Time to plateau	0.44NS	1.96NS	1.10NS	7.20*	3.38NS
Slope to 0.8 HR	2.49NS	1.20NS	3.74NS	1.52NS	0.17NS
Slope to plateau	0.69NS	9.85**	16.97**	8.67**	0.16NS
Avg PP pre-tilt	0.42NS	3.90NS	2.96NS	0.03NS	0.98NS
Min PP during tilt	0.81NS	0.03NS	4.46*	1.25NS	2.96NS
Avg pre PP-min during	0.56NS	1.66NS	8.45**	1.47NS	2.45NS
Frac decrease in PP	0.76NS	0.61NS	6.26*	1.50NS	2.77NS
Time of min PP	3.43NS	6.88*	0.11NS	0.41NS	4.34*
Avg pre mean-min dur	1.23NS	3.65NS	9.81**	2.48NS	1.29NS
Slope of diastolic BP	1.83NS	0.45NS	7.94**	5.09*	1.07NS
Slope of systolic BP	2.82NS	0.16NS	3.19NS	3.66NS	0.69NS
Slope of mean pressure	2.39NS	0.30NS	5.58*	4.60*	0.92NS
Slope of PP	3.03NS	0.02NS	0.32NS	1.11NS	0.17NS

* $p < 0.05$

** $p < 0.01$

NS   Non-significant

TABLE III

Means of Measurements from Tilt Table Data*

Measurement	Pre De-conditioning	Post Bed-rest	Post Bed-rest with Cuffs	Post Bed-rest with Exercise
Time to tilt down	23.9	21.0	17.4	19.0
Avg HR pre-tilt	64.1	66.5	66.1	64.0
Max HR during tilt	97.8	119.7	111.9	119.0
Min HR after tilt	54.7	58.8	58.6	58.1
Cng in HR with tilt	33.7	53.1	45.8	55.0
Frac incr in HR	0.53	0.81	0.71	0.87
Avg pre HR-avg post	6.8	4.6	5.2	3.1
Time of max HR	12.2	11.8	8.0	10.0
Time to 0.8 max	6.4	5.8	3.9	5.0
Time to plateau	3.3	4.1	2.8	5.0
Slope to 0.8 HR	6.5	9.0	10.9	9.6
Slope to plateau	5.2	8.3	9.4	8.9
Avg PP pre-tilt	56.0	61.0	60.0	57.0
Min PP during tilt	31.0	30.0	21.0	26.0
Avg pre PP-min dur	25.0	31.0	39.0	31.0
Frac decr in PP	0.45	0.51	0.65	0.54
Time of min PP	8.4	13.9	7.7	10.0
Avg pre mean-min dur	27.0	41.0	50.0	38.0
Slope of diastolic BP	-1.1	-1.8	-4.7	-3.9
Slope of systolic BP	-2.0	-3.0	-6.4	-6.1
Slope of mean pres	-1.3	-2.2	-5.3	-4.6
Slope of PP	-0.9	-1.2	-1.8	-2.2

*Units are indicated in text.

In table III are presented the means of measurements for the different conditions. The prerecumbency tilts were pooled and the post-treatment (during recumbency) tilt mean measurements are presented for each treatment. The units of the various measurements are as follows: pressure (mm Hg), heart rate (beats/minute), slope of heart rate (beats/minute/minute), and the slope of pressure (mm Hg/minute). These data are presented to indicate trends of change in the measurements even though there was no statistical difference in the three post-treatment tilt table procedures. The direction of change in measurements after the three potential treatments (during bedrest) is indicative of the changes that characterize the deconditioning of bedrest.

In table IV are presented the means of measurements obtained during the tilt procedures which compare the response of nonathletes and athletes. There were some differences in the two groups before deconditioning. However, both groups showed the same general pattern of changes characterizing deconditioning.

DISCUSSION

The average heart rate pretilt showed a small but nonsignificant increase after the recumbency periods during which treatment measures were used. This failure to observe an increase in heart rate is different from the increased rates observed by others, and may be because of the short period of recumbency. Likewise, there was but a small difference in the resting heart rate of the athletes compared with the nonathletes. However, all subjects were in good physical condition, and the resting heart rates were low for both groups. The nonathlete/athlete distinction had been made initially on the basis of the medical history of participation in physically competitive sports and an active exercise program.

The failure to observe a significant protective effect from use of leg cuffs, as has been found with extremity cuffs used with water immersion, could have been a result of the use of different inflation-deflation cycles, use of leg cuffs only, or differences in the mechanism of deconditioning for bedrest and water immersion. Vogt has suggested that the protective effect of cuffs in water immersion studies may occur with arm cuffs only, and Vogt and Johnson have suggested a possible mechanism to account for the changes. Further studies on cuff timing cycles and use of cuffs on arms and legs only during water immersion are needed to define the reason for the differences observed.

The failure to observe a significant protective effect from the periodic exercises could be explained in more than one way. Either the

TABLE IV

Table of Means of Measurements from Tilt Table Studies
to Compare Non-athletes and Athletes*

Measurement	Non-athlete		Athlete	
	Pre**	Post**	Pre**	Post**
Time to tilt down	23.9	17.6	23.8	21.1
Avg HR pre-tilt	65.0	67.5	63.0	63.1
Max HR during tilt	102.3	119.1	92.2	114.0
Min HR after tilt	56.8	61.7	52.1	54.5
Cng in HR with tilt	37.3	51.7	29.2	50.9
Frac incr in HR	0.50	0.78	0.46	0.82
Avg pre HR-avg post	5.74	3.12	8.12	5.73
Time of max HR	13.3	8.5	10.7	11.8
Time to 0.8 max	6.27	5.53	6.67	4.08
Time to plateau	3.13	4.20	3.50	3.67
Slope to 0.8 HR	7.50	9.08	5.28	10.8
Slope to plateau	5.46	8.16	4.94	9.72
Avg PP pre-tilt	53.6	58.5	58.3	60.0
Min PP during tilt	28.3	22.5	33.5	29.6
Avg pre PP-min dur	25.3	36.0	24.8	30.4
Frac decr in PP	0.47	0.62	0.42	0.50
Time of min PP	8.47	10.02	8.25	11.2
Avg pre mean-min dur	27.7	51.8	25.0	31.9
Slope of diastolic BP	-1.14	-3.71	-0.96	-3.13
Slope of systolic BP	-1.66	-5.95	-2.42	-4.18
Slope of mean pressure	-1.31	-4.46	-1.45	-3.48
Slope of PP	-0.52	-2.24	-1.45	-1.05

*Units are indicated in text.
**All tilts pre are pooled, all tilts post are pooled.

dose may have been inadequate, or physical inactivity may not be the principal factor accounting for the changes observed in the tilt table test. Vallbona and associates have reported a suggestive protective effect from periodic large doses of isometric exercise during 14 days of bed recumbency. Miller observed no increased benefit from the use of in-bed exercises during 2 weeks of recumbency.

The use of an objective approach in the analysis of tilt table data collected during controlled experimental circumstances provides a significant aid in the interpretation of tilt table data. Such is especially the case where there is a need to detect and interpret changes in tilt table responses that are directly attributable to the procedure or treatment measure, and there is need to distinguish normal variations in response from repeated tilt procedures on a given subject or group of subjects.

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THE EFFECTIVENESS OF EXTREMITY CUFFS IN PREVENTING CARDIOVASCULAR

DECONDITIONING ASSOCIATED WITH TWELVE HOURS OF WATER IMMERSION

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Studies have been conducted that demonstrate cardiovascular deconditioning occurs with prolonged bedrest, water immersion, chair rest, or space flight. The mechanism or mechanisms responsible for the cardiovascular deconditioning seen with each of these situations is not clear. The lack of knowledge on the mechanism of deterioration of the cardiovascular system has made research on preventive and control measures difficult.

Graveline in 1963 showed a protective effect against the tilt table intolerance seen after water immersion by the use of extremity cuffs intermittently inflated using a 1-minute-on, 1-minute-off inflation-deflation cycle. Vogt, in bedrest studies conducted in 1964, did not demonstrate a protective effort of lower extremity cuffs intermittently inflated using a 5-minute-on, 10-minute-off inflation-deflation cycle. Vogt did confirm a protective effort from extremity cuffs inflated with a 1-minute-on, 1-minute-off, inflation-deflation cycle. And, because of the experimental design, interpreted the results as being due primarily to the cuffs inflated on the upper extremity. Vogt and Johnson found an increased rate of disappearance of tagged albumin from the vascular system and a decline in plasma volume during water immersion, and suggested this as one possible contributing mechanism for the cardiovascular deconditioning seen with water immersion. The use of the extremity cuffs reduced the rate of disappearance of the tagged albumin and protected against the loss of plasma volume.

It was the purpose of the experiment to further study the mechanism of the protective effect seen with the use of intermittently inflated extremity cuffs by comparing different cuff configuration and inflation times on the same group of subjects who underwent repeated water immersion experiments.

METHOD

Subjects

Nine healthy adult male subjects participated in this study which involved eight experimental conditions. Subject B.J.H. participated only in the first two water immersion conditions and was replaced by subject J.Z.H. for the remainder of the test conditions. For each subject a complete medical history was compiled and a physical examination (with appropriate laboratory tests) was performed to exclude subjects with any conditions contraindicatory to their participation in the study. Some anthropometric measurements and the subject occupations are presented in table I.

Experimental Design

Table II shows the eight experimental conditions in which the subjects participated. The duration of each of these experimental conditions was 12 hours. For convenience of testing, the subjects were divided into two groups. Group A consisted of subjects R.L.A., L.F.E., G.G.G., and A.J.P., and Group B consisted of subjects L.E.D., B.G.H., J.Z.H., A.C.I., and H.G.R. Table III presents the assignment of experimental condition to each group, for each of the eight experimental conditions in the study.

Experimental Protocol

The subjects were admitted to the Texas Institute for Rehabilitation and Research as hospital patients for experimental studies. They remained in the hospital for a 2-month period. Three days prior to the first immersion period, the subjects were started on a controlled diet approximating 8 to 10 grams salt intake daily and were required to spend the night in the hospital. At times during the day when the subjects were not undergoing testing or participating in experimental studies they were allowed to come and go from the hospital. They were required to eat all meals in the experimental ward, sleep at night in the ward, and keep an activity schedule approximating their schedule prior to being hospitalized.

TABLE I

SUBJECTS

Initials	Age	Height (cm.)	Weight (kg.)	Occupation
A.J.P.	22	185	74.8	Marine veteran *
G.G.G.	28	172	55.7	Shop clerk
B.G.H.	22	174	88.9	Laborer
H.G.R.	28	175	77.8	Marine veteran *
R.L.A.	21	187	82.0	Student
L.F.E.	25	185	81.7	Student athlete
A.C.I.	24	163	54.3	Student athlete
L.E.D.	22	187	77.0	Army veteran *
J.Z.H.	27	183	73.4	Aircraft mechanic

* Unemployed

TABLE II

EXPERIMENTAL CONDITIONS

1   Water Immersion (W.I.)

2   W.I., Arm Cuffs only

3   W.I., Leg Cuffs only

4   W.I., Arm and Leg Cuffs

5   Bed Rest – 12 hours

6   Chair Rest – 12 hours

7   W.I., Leg Cuffs, last
    4 hrs. W.I., 120 mm. Hg

8   W.I., Leg Cuffs, 15 min./hr.
    for 12 hrs. at 120 mm. Hg

TABLE III

SCHEDULE OF EXPERIMENTS

Week	Group A	Group B
1	1	2
2	3	1
3	5	6
4	6	5
5	8	7
6	7	8
7	2	3
8	4	4

At 5 p.m. on the day of conducting an experimental condition, the subjects were fed a usual hospital meal, after which they were given no further food or water until the beginning of the experiment, which started at 10 p.m. that night and lasted until 10 a.m. the following morning. At 10 p.m., the beginning of the experimental test condition, the subjects were given 400 ml of water. They were later fed a 400 ml malt at 2 a.m. and 8 a.m. during the experimental condition. Group A was tested on Monday night of each week, whereas group B was tested the following night using the random assignment of experimental conditions shown in table III.

All experimental conditions were of 12 hours duration. For the water immersion studies, the subjects were immersed in the head-out position, utilizing a life preserver around their necks with a strap encircling the buttocks to provide a bouyant effect to keep them in a semi-sitting position without requiring exertion or muscular effort by the subject. The temperature of the water was maintained at 93 degrees Fahrenheit ± 1 degree Fahrenheit. For the bedrest condition, the same pre-experimental conditions were used, and the subject was admitted to bedrest instead of water immersion. For the chair rest experiment, the subjects sat in office-desk-type chairs for the 12-hour period, during which time they were allowed to read a book. At the beginning and end of each experimental condition, the subject was weighed, after he had emptied his bladder, using a platform scale with a resolution of ±50 grams.

Prior to the experiment, at 3 hours, 6 hours, and at the termination of the experiment, the following measurements were made: serum sodium, serum potassium, serum protein electrophoresis, serum osmolality, and hematocrit. Prior to and after each experimental condition, plasma volume determinations were performed using iodinated human serum albumin (I^{125} and I^{131}). In addition to these determinations, the disappearance rate of isotope from the plasma was determined by counting the radioactivity of a 1 ml sample of plasma which was drawn at 3, 6, and 12 hours after the initial plasma volume determination made at the beginning of each experiment. Urine was collected and aliquots were taken for determining radioactivity excreted in the urine. Urine samples were collected at 3, 6, 9, and 12 hours of each experimental condition and the volume and specific gravity were recorded. The samples collected at 9 and 12 hours were pooled. Thus, three samples were collected for the following periods: (a) 0 - 3 hours, (b) 3 - 6 hours, (c) 6 - 12 hours. The following laboratory tests were performed: (a) sodium, (b) potassium, (c) urea, (d) osmolality, and (e) the dip stick test for urine protein.

For the water immersion studies, the arm and leg cuffs were in-
flated from separate sources of pressure; the arm cuffs were inflated
to a pressure of approximately 60 to 70 mm Hg, and the leg cuffs were
inflated to a pressure of 120 mm Hg to compensate for the balancing
hydrostatic pressure effect due to the weight of the water above the
level of the leg cuffs. Cuff treatment was employed as indicated,
using a 3.75-inch-wide cuff applied to the upper part of the thigh and
arm depending upon the experimental condition. The cuff inflation-
deflation cycle was 2 minutes on, 4 minutes off, with the cuff being
fully inflated in 5 to 8 seconds, throughout the 12-hour period for
the experimental conditions, (a) arm cuffs only, (b) leg cuffs only,
(c) both arm and leg cuffs. For the condition of leg cuffs only for
the last 4 hours of immersion, the leg cuffs were inflated to a pres-
sure of 120 mm Hg for the last 4 hours of immersion using the same
2-minutes on, 4-minutes off cycle. For the experimental condition of
leg cuffs for 15 minutes per hour for 12 hours, the leg cuffs were in-
flated through three 2-minutes-on, 4-minutes-off cycles each hour with
an inflation pressure of 120 mm Hg. No cuff treatment was employed
during the bedrest and chair rest experimental conditions.

Tilt Table Studies

Tilt table studies were performed before and after each experi-
mental condition. In order to avoid the influence of circadian varia-
tions upon tilt response, the tilt prior to a given experimental condi-
tion was performed at approximately 2 p.m. the afternoon prior to the
subjects' participation in the experiment which began at 10 p.m. that
night. The subjects were tilted on completion of the experimental con-
dition at 10 a.m. the following day. After the subject was considered
to be in a baseline condition for the particular test circumstance,
5 minutes of control data were obtained with the subject in the hori-
zontal position. The subject then was tilted manually in approximately
3 to 5 seconds to a 70° head-up tilt position. The subject was supported
in the upright position by an English-saddle type support with most of
his body weight borne by his ischael tuberosities, thus providing a
passive tilt. The subject was kept in the upright position for
20 minutes unless syncope or impending syncope occurred. After tilt
down, an additional 5 minutes of control data were obtained.

Data were obtained continuously during the tilt procedure and re-
corded on a strip chart recorder and on magnetic tape for storage and
future analysis. For electrocardiographic data, NASA-type electrodes
were placed at the M-X and transthoracic sites. Respiration was mea-
sured with an impedance pneumograph connected transthoracically.

Cuff-microphone blood pressure measurements were obtained from the
right arm, using apparatus to obtain automatic cuff inflation, cycled
every 30 seconds.

Data Analysis

A complete statistical analysis of all data obtained in this ex-
periment has not been completed at present. The results presented here
are preliminary to a complete report, which will be submitted to the
Journal of Aerospace Medicine in the near future.

The tilt table heart rate data were determined by counting the
total heart beats in each successive minute during the tilt procedure.
Blood pressure measurements were arbitrarily and systematically collected
exactly at the beginning of each minute by reading the corresponding
systolic and diastolic pressure. These heart rate and blood pressure
data were analyzed by an objective approach described in another paper.
For the heart rate and blood pressure information, a group of derived
measurements were set up which would characterize the tilt response.
An analysis of variance then was performed to select statistically
significant changes which might characterize the effect of different
treatments. The units for the derived measurements are as follows:
heart rate (beats per minute), blood pressure (mm Hg), slopes of heart
rate (beats per minute per minute), slopes of blood pressure (mm Hg per
minute), and time (minutes). The analysis of blood volume and other
data utilized analysis of variance, with the main effects of subject and
treatment; also considered in the analysis was the interaction between
the main effects.

RESULTS

The results of the 128 separate tilt table tests are too voluminous
to present individually in this report. Only a summary of the analysis
of variance and a table of means for the experimental procedures will
be presented. In table IV is presented the F values and levels of sig-
nificance for heart rate and blood pressure variables for different
experimental circumstances. The comparison of the eight preexperimental
tilt table tests on each subject is shown in column one of table IV.
For these pooled tilt table tests, conducted on different days, only
1 of the 22 variables considered showed a statistically significant
difference. For the analysis performed here, the preexperiment 64 tilt
table tests were pooled for comparison with the tilt table tests after
each of the eight experimental conditions. The results are indicated

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TABLE IV

F Values and Levels of Significance of Tilt Table Variables for
Different Experimental Circumstances

Variable	Pooled Pre Test	Chair Rest	Bed Rest	Arm Cuffs	Arm/Leg Cuffs	Leg Cuffs Last 4hr.	Water Immersion	Leg Cuffs	Leg Cuffs 15/Hour
Time to Tilt Down	0.86	0.25	6.49*	7.37**	5.57*	3.11	19.74**	8.37**	51.83**
Avg HR Pre Tilt	0.87	1.96	1.30	1.34	1.54	2.68	2.23	0.28	2.53
Max HR During Tilt	0.58	4.23*	0.04	2.98	0.99	1.62	3.70	6.85*	0.14
Min HR After Tilt	0.28	0.90	2.04	1.80	0.01	1.66	2.98	0.00	1.94
Cng in HR With Tilt	0.21	0.98	1.12	13.33**	8.35**	13.33**	18.18**	16.62**	5.91*
Frac Incr in HR	0.40	0.14	1.35	11.08**	7.37**	11.79**	15.33**	10.82**	6.89*
Avg Pre HR Avg Post	1.46	0.11	0.61	0.00	3.94	1.43	0.86	2.73	0.10
Time of Max HR	0.63	0.02	2.61	0.07	0.08	0.11	0.11	1.23	2.41
Time to .8 Max HR	0.53	2.38	0.31	0.09	0.21	0.24	0.05	0.16	0.00
Time to Plateau	1.08	0.08	0.15	2.17	0.15	3.84	7.46**	0.00	0.15
Slope to .8 HR	0.78	2.41	0.02	0.71	0.86	1.30	1.73	2.12	5.53*
Slope to Plateau	0.70	2.31	5.39*	7.40**	11.07**	7.72**	6.86*	15.63**	15.12**
Avg PP Pre Tilt	1.76	0.34	0.68	0.66	2.35	4.20*	5.01*	4.00*	4.67*
Min PP During Tilt	1.00	0.98	0.08	4.20*	8.21**	16.38**	10.33**	10.36**	10.36**
Avg Pre PP Min During	0.55	0.12	0.42	1.25	0.91	2.84	0.37	0.84	0.39
Frac Decr in PP	0.44	1.11	0.00	4.36*	4.58*	15.59**	6.76*	8.00**	5.64*
Time of Min PP	0.74	0.18	0.17	0.52	0.00	1.30	0.58	2.34	0.36
Avg Pre Mean - Min During	4.51**	1.25	0.00	0.01	2.20	1.21	1.32	2.17	7.51**
Slope of Diastolic	1.09	0.33	3.85	0.54	1.00	0.15	8.01**	3.46	16.13**
Slope of Systolic	0.60	1.77	3.68	2.11	3.57	1.38	3.43	13.78**	18.47**
Slope of Mean Press	0.57	1.01	4.51*	1.63	2.34	0.63	7.04**	8.73**	18.04**
Slope of Pulse Press	1.77	0.70	0.37	1.17	1.11	——	0.31	5.84*	12.72**

in table IV in columns 2, 3, 4, 5, 6, 7, 8, and 9 of the experimental
condition in terms of severity of deconditioning, going from chair rest
to leg cuffs 15 minutes per hour.

As indicated in table IV, the only significant variable different
after the chair rest experiment is the initial heart rate during tilt.
Several more variables become statistically significant comparing the
tilts performed before and after the experimental circumstances, for
each experimental condition as it is presented in the table. Table V
presents the table of means (uncorrected) of the variables considered
in table IV.

It should be noted that the statistically significant difference
($p < 0.05$) of the maximum heart rate during tilt after chair rest com-
pared to the pooled pre-test tilts resulted from a lower maximum heart
rate after chair rest compared to the other tilts. This should be dis-
tinguished from the water immersion experiments in which all showed a
higher maximum heart rate during tilt after the deconditioning experi-
ment. It also should be noted that the trend of measurements for
nearly all the variables considered is opposite for chair rest compared
to bedrest and water immersion experiments.

The results presented in tables IV and V, for arm cuffs and arm
plus leg cuffs, indicate that there are definite changes after the de-
conditioning experiments but these changes are of less magnitude than
for the other four water immersion experiments considered. Very little
distinction can be made by the present analysis as to the difference in
severity of deconditioning for the last four experimental conditions of
leg cuffs for the last 4 hours, water immersion, leg cuffs for the en-
tire 12 hours, and leg cuffs 15 minutes per hour for the 12-hour-duration
period.

The average heart rate pretilt after deconditioning was not statis-
tically different from the heart rate pretilt for the pooled control
tilts, although the table of means indicates a slightly lower value after
all experimental conditions. Some of this decrease could be related to
the time of day difference in the performance of tilt, although there
was not more than 4 hours difference as set up in the experimental de-
sign. The tilts were performed after the deconditioning experiments
prior to lunch, whereas the control tilts were performed after lunch.
It should be noted that change in heart rate with tilt, and percentage
increase in heart rate with tilt were two of the more sensitive heart
rate indicators of the changes after deconditioning compared to control
values. The average pulse pressure pretilt, the minimum pulse pressure
during tilt, and the fractional decrease in pulse pressure during tilt
also were significant indicators of the deconditioning of water immer-
sion. Slopes of blood pressure were not as sensitive indicators as were

TABLE V

Table of Means (uncorrected) for Variables Presented in Table IV

Variable	Pooled Pre-Test	Chair Rest	Bed Rest	Arm Cuffs	Arm/Leg Cuffs	Legs Last 4 Hours	Water Immersion	Leg Cuffs	Leg Cuffs 15/hour
Time to Tilt Down	25.9	26.0	24.7	24.1	25.0	25.4	23.0	25.1	20.4
Avg HR Pre-tilt	70.8	65.7	66.6	66.4	66.1	64.8	65.2	68.8	64.7
Max HR During Tilt	98.1	89.8	97.3	105.3	102.3	103.1	105.9	109.1	99.6
Min HR After Tilt	61.9	58.0	56.0	56.4	61.5	56.6	54.6	62.1	56.1
Cng in HR With Tilt	27.2	24.1	30.7	38.9	36.2	38.4	40.7	40.3	34.9
Frac Incr in HR	0.39	0.38	0.47	0.61	0.56	0.61	0.6	0.6	0.6
Avg Pre HR - Avg Post	6.9	6.2	8.5	6.9	2.6	4.4	8.8	3.4	6.2
Time of Max HR	10.7	10.4	6.6	10.0	10.0	9.9	9.9	7.7	6.8
Time to 0.8 Max HR	4.1	6.9	3.1	3.6	3.3	5.0	4.5	4.8	4.2
Time to Plateau	3.1	3.3	3.0	3.8	3.0	4.0	4.8	3.1	3.0
Slope to 0.8 HR	9.6	4.9	9.2	12.3	12.5	13.4	14.0	14.2	17.5
Slope to Plateau	4.8	3.7	6.5	6.7	7.1	6.8	6.8	7.7	7.9
Avg PP Pre-tilt	57.3	55.2	54.5	54.5	51.8	50.3	49.6	50.4	49.6
Min PP During Tilt	28.4	25.3	27.5	22.3	19.9	16.4	18.9	18.7	18.8
Avg Pre PP - Min During	28.9	29.9	27.0	32.2	32.0	34.0	30.7	31.7	30.9
Frac Decr in PP	0.50	0.55	0.51	0.59	0.60	0.67	0.62	0.63	0.61
Time of Min PP	10.1	11.1	11.1	8.5	10.1	12.8	11.9	13.6	8.7
Avg Pre Mean - Min During	5.0	1.8	4.9	5.2	0.4	8.3	8.4	9.3	13.5
Slope of Diastolic	0.102	0.200	-0.316	-0.024	-0.079	0.029	-0.606	-0.235	-1.496
Slope of Systolic	-0.178	0.089	-0.727	-0.604	-0.573	-0.474	-0.759	-1.025	-2.996
Slope of Mean Press	0.009	0.163	-0.453	-0.217	-0.243	-0.139	-0.657	-0.498	-1.996
Slope of Pluse Press	-0.281	-0.111	-0.411	-0.580	-0.494	-0.503	-0.154	-0.790	-1.500

the other measures of the deconditioning demonstrated by the analytic technique used but the slopes show significant differences as the deconditioning becomes more severe.

Table VI presents the documentation of the occurrence of syncope in the nine experimental subjects showing the occurrence of syncope pre- and postdeconditioning. In the 64 predeconditioning tilts, two subjects experienced syncope, whereas there were 13 occurrences of syncope or impending syncope after deconditioning.

Table VII indicates the weight changes of the subjects for the eight experimental conditions. There is variation from subject to subject in the gain or loss of weight but a definitely larger decrease in weight occurred in the experimental circumstance of water immersion without any protective device. A small increase in weight was noted for the experimental circumstance of chair rest.

In table VIII is shown the plasma isotope change for the various experimental circumstances ranked in the order of change in plasma volume after an experimental circumstance compared to the plasma volume before the experimental circumstance. The average plasma volume for all subjects was 3431 ml. A simple analysis of variance comparing the after plasma volume to the before plasma volume shows a statistical separation only of the first and last two experimental conditions at the 5 percent confidence level. A more sophisticated statistical analysis involving the study of other main effects and interactions is being performed to reduce the variance observed in the different experimental conditions to allow for a more confident statistical interpretation of the data collected in this study. It is noteworthy that the isotope disappearance rate showed a distinctive pattern, and followed the same general trend as the average change in plasma volume. The expected or normal isotope disappearance rate expressed as the percent of the radioactivity remaining after injection of the isotope is as follows: 3 hours, 85 percent; 6 hours, 78 percent; 12 hours, 65 percent. The total isotope appearing in the urine approximated 5 to 8 percent of the injected dose and does not show significant variation from experiment to experiment.

Preliminary analysis showed no statistically significant difference in the serum and sodium potassium for the different experimental conditions. Table IX presents the blood measurements associated with the plasma volume measurements. As indicated, there was an increase in hematocrit for all experimental circumstances, with the greatest increase occurring for the water immersion (without cuffs) condition, the experimental condition in which there was the greatest decline in plasma volume. Also indicated in table IX are the decreases in the total serum

TABLE VI

OCCURRENCE OF SYNCOPE

64 Tilts Pre   –   2

64 Tilts Post – 13

Subject	Syncope Pre/Post
AJP	0/1
GGG	0/0
BGH	0/1
HGR	1/1
RLA	0/0
LFE	0/2
ACI	0/0
LED	1/5
JZH	0/3

TABLE VII

WEIGHT CHANGE (Kg.)

Subject	W.I.	A	L	A+L	BR	CR	15/hr	Last 4 hr.
Allbright, R.	-1.8	-0.7	-0.4	-0.4	-0.3	-0.1	-0.6	-0.1
Elliott, L.	-1.6	-0.4	0.0	-0.6	+0.6	+0.4	-0.6	-0.6
Garcia, G.	-0.6	+0.4	+0.1	-0.2	0.0	+0.3	-0.2	+0.3
Patterson, A.	-0.3	+0.1	-0.7	-0.4	-1.1	-0.2	0.0	-0.3
Driver, L.	-0.2	-0.3	0.0	+0.4	-0.3	+0.2	-0.1	+0.4
Hays, J.	——	——	+0.6	-0.1	-0.4	-0.4	-0.6	-1.2
Hudson, B.	-0.3	+0.2	——	——	——	——	——	——
Irwin, A.	0.0	+0.1	0.0	0.0	-0.2	+0.1	+0.3	0.0
Roberts, H.	-0.1	-0.1	0.0	0.0	-0.4	-0.1	-1.0	-0.3
Average	-0.61	-.09	-0.05	-0.10	-0.26	+0.03	-0.35	-0.23

TABLE VIII

PLASMA ISOTOPE CHANGE

	$\triangle$PV (ml.)**	Isotope Disappearance* (% Remaining)
W.I.	563	48
Last 4 hrs.	494	54
15 min./hr.	481	57
B.R.	318	65
L.	283	59
A. & L.	272	59
A.	206	61
C.R.	151	70

* % remaining based on counting 1.0 ml. of plasma (with isotope mixed) at start and end of experiment; no correction made for total amount of plasma present. (3 hr., 85%; 6 hr., 78%; 12 hr., 65%)

** Average plasma volume for all subjects was 3431 ml.

TABLE IX

BLOOD MEASUREMENTS

	P.V. (ml. decr.)	Osm. (decr.)	Hct. (incr.)	Protein (decr.gm.%)	Albumin (decr.gm.%)
W.I.	563	5.5	4.7	0.56	0.60
Last 4 hr.	494	7.0	2.5	0.62	0.34
15/hr.	481	5.0	2.8	0.16	0.15
B.R.	318	2.3	3.3	0.67	0.67
L.	283	0.1	2.3	0.14	0.05
A.&L.	272	5.1	2.6	0.74	0.47
C.R.	151	(1.6)	2.5	0.26	0.13

protein and the albumin fraction indicated in terms of serum concentration. A decline in the serum osmolality also is noted for all experimental conditions except the chair-rest study. A complete statistical analysis of the protein electrophoresis has not been performed at this time, and the results will not be discussed.

Table X presents the average urine volume for each experimental treatment with the first column indicating the 12-hour urine volume; the ranking in order of total volume for each experimental condition is indicated in the parenthesis beside the volume. The volumes for the first 3 hours and the second 3 hours of the experimental circumstance are indicated in the second and third columns of table X. It is interesting to note that the urine volume for the first 3 hours of water immersion is greater than for the experimental condition of water immersion with leg cuffs for the last 4 hours, although the volume for the 3 - 6 hour collection period was increased in the later experiment. In table XI is presented the urine osmolarity and associated urine volume measurements.

DISCUSSION

A complete evaluation and interpretation of the results of this experiment connot be made until the statistical analyses are completed on all of the data collected.

The general observations and conclusions which can be made at present are as follows:

1. Twelve hours of water immersion produces definite cardiovascular deconditioning as manifested by the tilt table response and plasma volume change.

2. Chair rest of 12 hours duration produces a change, which has a trend opposite to bedrest and water immersion.

3. A diuresis occurred in the water immersion experiments, which did not utilize cuffs.

4. Arm cuffs cycles 2-minutes-on, 4-minutes-off, provide a protective effect against cardiovascular deconditioning of water immersion; the value of leg cuffs could not be determined from the statistical analysis performed.

5. Changes in serum and urine measurements not observed with 6 hours of immersion were observed in association with 12 hours of immersion.

6. No inference can be made as to the cardiovascular potential protective effect of arm cuffs for the experimental conditions of bed-rest or space flight.

TABLE X

Average Urine Volume for Experimental Treatments

Treatment	Volume (ml.)		
	Total 12 hrs.	0-3 hrs.	3-6 hrs.
Water Immersion (W.I.)	1010 (1)	372	291
W.I., Arm Cuffs only	463 (7)	159	99
W.I., Leg Cuffs only	791 (3)	206	172
W.I., Arm and Leg Cuff	544 (6)	194	166
Bed Rest – 12 hours	674 (4)	232	188
Chair Rest – 12 hours	452 (8)	103	206
W.I., Leg Cuffs, last 4 hrs. of Immersion (120 mm. Hg)	657 (5)	264	320
W.I., Leg Cuffs, 15 min./hr. for 12 hrs. at 120 mm. Hg	912 (2)	226	319

TABLE XI

URINE OSMOLARITY AND VOLUME

Treatment	Osmolarity (mOsm/sample)	Urine Volume (ml.)
8	1871	912
1	1700	1009
5	1617	674
3	1608	791
7	1484	656
4	1343	544
6	1240	451
2	1169	463

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THE EFFECTS OF ACUTE HEAT STRESS ON CARDIAC OUTPUT

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INTRODUCTION

Despite the fact that the physiological responses to various environmental temperatures have been the subject of many reports in the past, controversy continues to exist regarding the role of cardiac output, oxygen consumption and arteriovenous oxygen differences in man's adaptation to acute heat stress. It has become increasingly evident that part of the discrepancy between conclusions has resulted from variations in the methodology used, the type of subjects tested and the environmental conditions under which subjects were tested.

This paper reports on the hemodynamic responses obtained in fifteen normal untrained male volunteer subjects who were studied at supine rest and exercise in a comfortable environment and at three different temperature levels. A comparison of measurements obtained in this manner should provide a more clear and valid insight into the hemodynamic changes which occur during acute heat stress.

METHODS

Studies on fifteen normal unacclimatized male volunteer subjects between the ages of 27 and 42 (average age is 34) form the basis of this report. The subjects were admitted to the hospital prior to the study and were judged to be in good health following a careful history, physical examination, routine laboratory studies that included chest X-ray, resting electrocardiogram and routine pulmonary function testing. The volunteers were familiarized with the study by participating in a practice run of the entire procedure prior to the study. All measurements were made in the post-absorptive, nonsedated state. Fifteen subjects were studied in a climatic chamber at a comfortable environment and after 1-1/2 hours of acute heat exposure. Five subjects were studied

at 78° F and 100° F, five subjects at 78° F and 115° F, and five sub-
jects at 78° F and 125° F. Relative humidity was held constant at
approximately 42 percent for all studies. Right heart catheterization
was performed under local anesthesia and used a left antecubital vein.
A no. 8 single lumen cardiac catheter was advanced under fluoroscopic
and electrocardiographic control to the main pulmonary artery position.
The left brachial artery was cannulated with a no. 18 Cournand needle.
Cardiac outputs were measured by the direct Fick Method during the 4th
and 6th minutes in the supine resting and exercise positions at all
temperature ranges. Arterial pressures were measured over two respira-
tory cycles by using a Statham strain gauge transducer leveled 5 cm
below the sternal angle. Heart rates were recorded electrocardio-
graphically throughout the study. All recordings were made on the
Electronics for Medicine at a paper speed of 25 mm/sec. Expired air
was analyzed for oxygen and carbon dioxide by micro-Scholander analysis.
Arterial and mixed venous blood samples were drawn simultaneously with
the gas collection and were analyzed in duplicate for oxygen content by
the Van Slyke and Neil Methods.

RESULTS

Table I depicts the mean values for five subjects studied during
supine rest and exercise at 78° F and 100° F. A comparison of the two
resting studies reveals no significant differences in the oxygen con-
sumption, cardiac output, cardiac index and arteriovenous oxygen dif-
ference. Similarly, no significant differences were observed in the
mean values when these five subjects performed comparable levels of
supine exercise at both of these temperatures. All subjects responded
with a slight increase in heart rate upon exposure to this degree of
ambient temperature. No significant changes in body weight or body
temperature occurred in any of the subjects.

The results of five subjects studied at 78° and 115° F are shown
in table II. A comparison of the resting studies reveals that the mean
cardiac output value at 115° F is increased. Mean A-V oxygen differ-
ences for the two resting studies are the same. However, two of the
five subjects studied at 115° F were not in a basal state and, thus,
the mean values for cardiac output are considered spuriously high.
Once again exposure to acute heat stress produced an increase in heart
rate.

The results of exercise in these five normal subjects reveal that
at nearly comparable levels of oxygen consumption, the arteriovenous
oxygen difference begins to narrow and the cardiac output is increased
at 115° F.

RESULTS OF FIVE NORMAL SUBJECTS

TABLE I

TESTED AT 78°F. AND 100°F.

MEAN VALUES	REST Temp. 78°F.	REST Temp. 100°F.	EXERCISE 50 WATTS Temp. 78°F.	EXERCISE 50 WATTS Temp. 100°F.
OXYGEN CONSUMPTION ML/MIN/M^2	131 ± 18	138 ± 17	381 ± 45	373 ± 56
CARDIAC OUTPUT L/MIN.	5.48 ± 0.8	5.60 ± 0.3	9.25 ± 1.7	8.84 ± 2.0
CARDIAC INDEX L/MIN.	2.80 ± 0.2	2.87 ± 0.1	4.74 ± 0.7	4.56 ± 1.2
STROKE VOLUME (ML.)	83 ± 10	76 ± 9	89 ± 17	81 ± 23
HEART RATE	65 ± 5	75 ± 9	105 ± 9	113 ± 3
ARTERIOVENOUS OXYGEN DIFF. (VOL.%)	4.5 ± 0.3	3.6 ± 0.4	7.9 ± 0.8	7.3 ± 1.0

RESULTS OF FIVE NORMAL SUBJECTS

TABLE 2

TESTED AT 78°F. AND 115°F.

MEAN VALUES	REST Temp. 78°F.	REST Temp. 115°F	EXERCISE 50 Watts Temp. 78°F.	EXERCISE 50 Watts Temp. 115°F.
OXYGEN CONSUMPTION ML/MIN/M^2	124 ± 19	151 ± 8	372 ± 33	374 ± 59
CARDIAC OUTPUT L/MIN.	6.45 ± 1.1	7.79 ± 0.7	10.76 ± 0.5	11.67 ± 1.3
CARDIAC INDEX L/MIN.	3.18 ± 0.3	3.81 ± 0.6	5.32 ± 0.4	5.78 ± 0.4
STROKE VOLUME (ML)	90 ± 12	75 ± 5	102 ± 7	88 ± 7
HEART RATE	70 ± 7	102 ± 7	105 ± 6	135 ± 13
ARTERIOVENOUS OXYGEN DIFF. (VOL.%)	3.9 ± 0.4	3.9 ± 0.4	7.0 ± 0.6	6.4 ± 0.5

These changes in cardiac output and arteriovenous oxygen differences become more manifest at higher temperatures. Table III compares the results of five normal subjects studied at ambient temperatures of 78° F and 125° F. In the resting studies at comparable oxygen consumption, cardiac output is significantly higher and arteriovenous oxygen difference is significantly lower at the higher temperature. These same changes in cardiac output and arteriovenous oxygen differences are noted for the exercise studies. Again at comparable oxygen consumptions the arteriovenous oxygen difference lowers from 8.4 vol percent to 6.8 vol percent, and the cardiac output increases from 11.55 L/min to 13.68 L/min. In both the resting and exercise studies, exposure to 125° F resulted in significant increases in heart rate in all subjects tested. At this temperature level all three subjects demonstrated changes in body weight and temperature. The range of weight loss was between 3 and 7 pounds and body temperature increased 1.7° F to 3.0° F.

DISCUSSION

In 1957 Burch and Hyman reported on the cardiovascular response of three normal resting subjects who were exposed for 1 to 2 hours to a hot and humid environment at 111° F and 87 percent RH. These investigators used the Fick principle and reported a four fold increase in cardiac output when normal subjects are exposed to this degree of thermal stress.

Sancetta in 1958, studied sixteen patients with a variety of cardiovascular diseases. These patients, who were sedated prior to the time of study, were exposed to a temperature of 98° F and 40 percent RH for a period of 2 hours. Sancetta concluded from his studies that exposure to an ambient temperature of 98° F and low humidity produces no increase in oxygen consumption, cardiac output, or arteriovenous oxygen difference.

Koroxenidis et al, reported a mean increase of 60 percent in cardiac output, a 49 percent increase in stroke volume, and a 9 percent increase in heart rate, in their study of eight normal resting subjects who were exposed to one level of acute heat stress. These authors attributed the increase of cardiac output to the increase in heart rate, which occurred in all subjects.

In the present study, cardioacceleration did occur in all subjects exposed to a hot environment. However, a significant increase in cardiac output was not evident until a temperature of 115° F was exceeded. Therefore, an increase in heart rate does not appear to be the reason

TABLE 3

RESULTS OF FIVE NORMAL SUBJECTS
TESTED AT 78°F. AND 125° F.

MEAN VALUES	REST TEMP. 78°F.	REST TEMP. 125°F.	EXERCISE 100 WATTS TEMP. 78°F	EXERCISE 100 WATTS TEMP. 125°F.
OXYGEN CONSUMPTION ML/MIN/M^2	122$\pm$17	129$\pm$19	477$\pm$39	483$\pm$42
CARDIAC OUTPUT L/MIN.	5.50$\pm$0.9	7.07$\pm$0.8	11.55$\pm$0.8	13.68$\pm$0.8
CARDIAC INDEX L/MIN.	2.84$\pm$0.3	3.53$\pm$0.5	5.90$\pm$0.4	6.98$\pm$1.1
STROKE VOLUME (ML.)	73$\pm$10	73$\pm$16	106$\pm$14	92$\pm$11
HEART RATE	77$\pm$11	101$\pm$16	108$\pm$7	157$\pm$14
ARTERIOVENOUS OXYGEN DIFF. (VOL.%)	4.5$\pm$0.4	3.6$\pm$0.2	8.1$\pm$0.4	7.1$\pm$0.6

for the increase in cardiac output. Furthermore, other studies per-
formed in our laboratory have confirmed the fact that in any given
state, changes in heart rate either above or below the sinus rate do
not alter the cardiac output.

However, it was apparent in the present study that the changes in
arteriovenous oxygen difference paralleled the observed increases in
cardiac output. These changes in A-V oxygen difference reflect periph-
eral adjustments of the body to maintain thermal balance. Exposure to
a hot environment results in an increase in skin blood flow, where there
is little loss of oxygen. Accordingly, the degree of unsaturation of
blood returning to the right side of the heart will be less.

In summary then, exposure to ambient temperatures above 115° F
results in an increase in cardiac output. This increase in cardiac
output is not caused by cardioacceleration. Furthermore, the cardiac
output changes are paralleled by inverse changes in A-V oxygen differ-
ences.

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CIRCADIAN RHYTHMS IN SIMULATED AND MANNED ORBITAL SPACEFLIGHT

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INTRODUCTION

The presence of biological rhythms in a rhythemic physical environment is not surprising. However, as was shown over 200 years ago, biological rhythms can continue when the organism is in a physical environment which most biologists consider constant with respect to living systems. This led to the hypothesis of a bioligical clock, which is thought to be present in organisms from protozoa to man. Although many of the basic properties of this biological clock have been defined, the underlying mechanism is still not thoroughly understood.

Most investigators subscribe to the theory that the biological clock is endogenous, with environmental factors such as light and temperature acting only as phase setters between the organism and the environment. One group of investigators, however, believes that these rhythms are the result of the organisms response to subtle daily geophysical fluctuations such as the earth's magnetic field. These latter investigations have been criticized on the basis of the statistical procedures used. However, there is no direct evidence in the literature that proved the endogenous theory. Thus, the question of an endogenous biological clock still awaits a scientific explanation.

There is another unsettled question regarding biological rhythms. How important are intact biological rhythms to overall homeostasis? Abnormal work-rest schedules as well as rapid movement across several time zones can disrupt biological rhythms and the performance of the travelers.

We have become interested in the study of human circadian rhythms in relation to the manned spaceflight program. This is an area in which both of the unanswered questions posed above are relevant. Manned spaceflight should provide information on the endogenous or ex-ogenous nature of the biological clock. The question of circadian dysrhythmia and possible performance decrements is also a pertinent question to the manned spaceflight program.

To evaluate these problems we are studying human biological rhythms and performance during simulated Apollo missions in conjunction with the Manned Spacecraft Center. Besides providing physiological and performance data during proposed work-rest schedules, it will also pro-vide baseline data for evaluation of any observed inflight disturbances which may occur, since we also have inflight experiments of biological rhythms planned for Apollo flights.

In particular we are looking at the relationship between perform-ance and three aspects of human circadian rhythms and these are indiv-idual variability during identical environmental conditions, the re-sponse of circadian rhythms to different environmental conditions, and the interrelationships of circadian rhythms within the same individual, or in other words, the circadian homeostasis.

This paper presents preliminary results of studies of human bio-logical rhythms within this framework. The data was obtained during a 30-day human isolation study as well as actual in-flight data from one of the Gemini flights.

METHODS

Four male university students whose ages were between 19 and 24 were kept in groups of two in specially designed chambers for a period of 30 days. Each chamber was 12 feet by 10 feet by 7 feet and was sealed from outside noise and light. A light intensity of 64 foot candles was controlled from outside the chambers. Cooking and sanita-tion facilities were provided inside the chambers.

Each subject wore an electrode vest which had provision for EKG, EEG, EOG, and body temperature measurements. Body temperature was measured by use of Benzinger ear probes, which were individually fitted for each subject. An electrode umbilical was attached to each vest and from there to an overhead track which allowed the subjects complete movement throughout the room.

Heart rate and body temperature were sampled for 1 minute every 10 minutes for each subject and digitized directly. One-hour samples were used for analysis.

Urine was collected in an automatic device which collected total urine voided over 6-hour periods. These were then converted to one-hour samples. The urine constituents of 17-OH corticosteroids, creatinine, osmolarity, sodium, potassium, and chloride were measured by standard clinical techniques.

Vigilance and time perception tests were administered twice each day to each subject. There were no watches allowed in the chambers nor were the subjects advised of the time.

The experimental lighting schedule was as follows: days 1 - 7, 16 hours light, 8 hours dark; days 8 - 15, 15.5 hours light, 8 hours dark; days 16-21, constant light.

Physiological and biochemical data were analyzed for periodicity by autocorrelation and power spectral techniques. The phase was derived by crosscorrelation with computer-generated sine waves. This was only applicable, however, when the autocorrelation showed a distinct circadian periodicity.

Gemini flight data was obtained from the onboard biomedical tape recorders. The EKG tapes were played through a calibrated cardiotack and heart rate read from this at hourly intervals. This data was analyzed in the same manner as that obtained in the isolation study.

RESULTS

Individual Variability

Figure 1 shows the autocorrelation function of body temperature for subject B during the first 5 days of the adaptation period. A very prominent circadian period is evident. Figure 2 shows the autocorrelation function of body temperature for subject A during the same period. There is no apparent circadian rhythm. Thus, two individuals under the same environmental conditions exhibited radically different circadian rhythms for this variable. One factor is the subjects daily routine before entering the chamber; however, this is not the only factor.
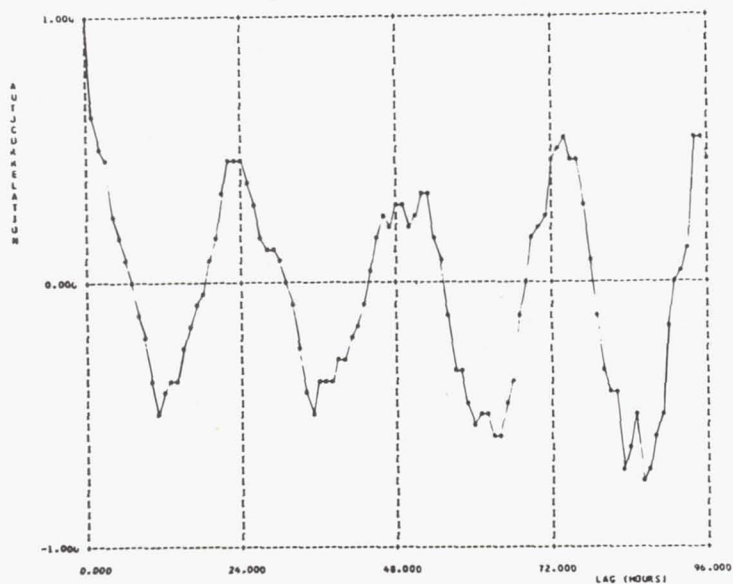
Figure 1. - Autocorrelation of body temperature for subject B during first 5 days of adaptation period.
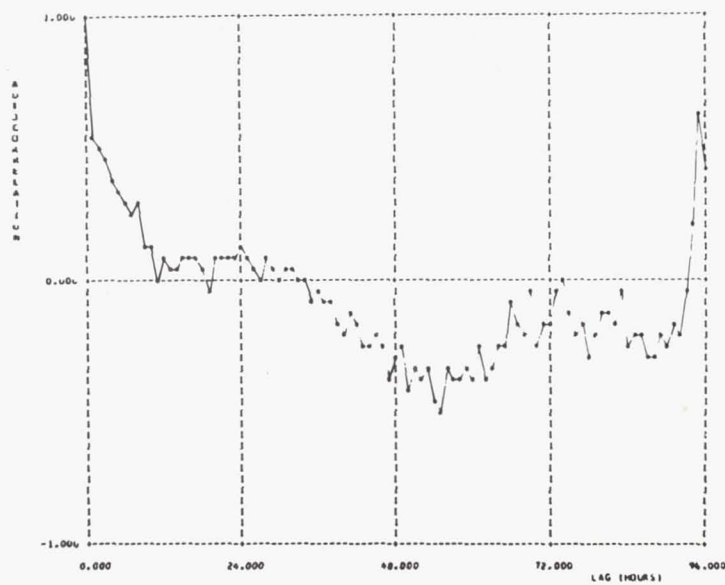
Figure 2. - Autocorrelation of body temperature for subject A during first 5 days of adaptation period.

Figure 3 shows the autocorrelation function of heart rate for one of the Gemini astronauts during flight. A prominent circadian rhythm is evident. Figure 4 shows the autocorrelation function for the other Gemini astronaut during the same flight. Although there is a slight circadian component, it is not nearly as pronounced as for the other astronaut. Since these two astronauts followed approximately the same schedules before and during the flight, this difference is probably a function of the individual.

Response to Different Lighting Schedules

Figure 5 shows the autocorrelation function for body temperature during the 23.5-hour day for subject A. A prominent circadian period of about 23 to 24 hours is evident. Another autocorrelation using the original 10-minute sample period did show a peak near 23.5 hours. Figure 6 shows the results obtained for the same subject and variable during 6 days of constant light. Complete disruption of the circadian rhythms is evident.

Differences in the rhythm of urine components were also observed during these experiments. Figure 7 shows the autocorrelation of 17-OH corticosteroids for subject A during the 23.5-hour lighting schedule. The prominent circadian period shown during this regimen is not disrupted during constant light as is seen in figure 8. Potassium, however, did not behave in this manner as is shown in figures 9 and 10. Whereas a prominent circadian period is evident during the 23.5-hour day, a period much greater than 25 hours seems to be prevalent during constant light.

Interrelationship of Circadian Rhythms

Figure 11 shows the autocorrelation function of all the parameters we were measuring for subject A during the adaptation period. As was shown before, the body temperature exhibits no prominent circadian component, whereas, heart rate does. Also notable is that the urine parameters seem to exhibit a period greater than 24 hours with the exception of potassium. This variable shows a period which is less than 24 hours. Thus, within one subject during the same time interval we find all possible combinations of human circadian rhythms; complete disruption, an exact 24-hour period, a period greater than 24 hours, and one less than 24 hours. That they can all be synchronized at one time is shown in figure 12 for the same subject during the next experimental period.

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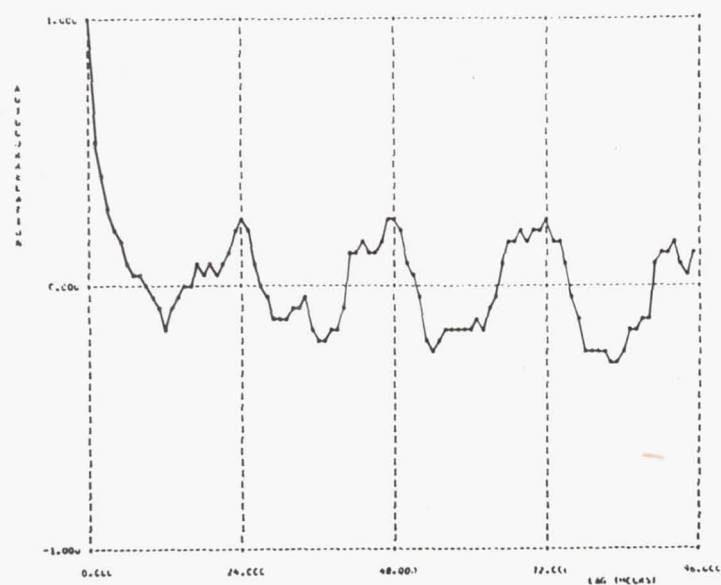
Figure 3. - Autocorrelation of heart rate for one of
Gemini astronauts during spaceflight.
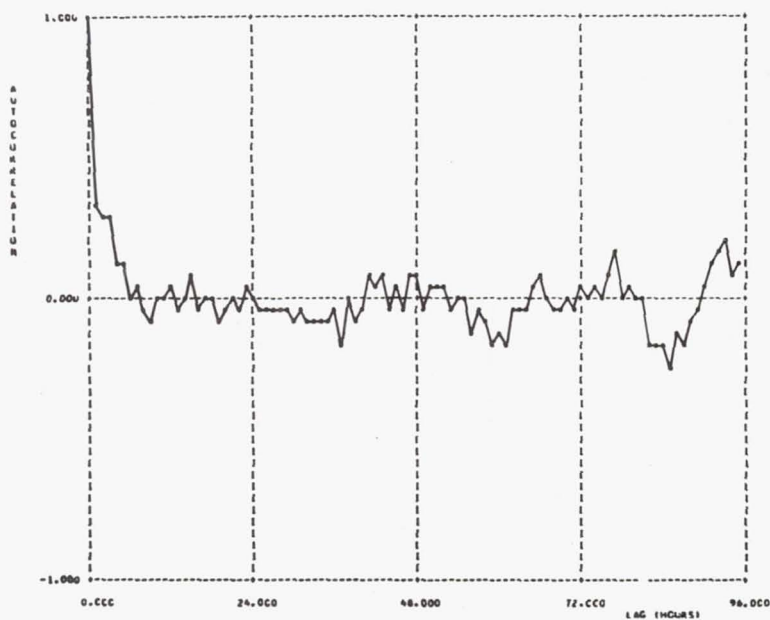
Figure 4. - Autocorrelation of second Gemini astronaut during
same flight as shown in figure 3.
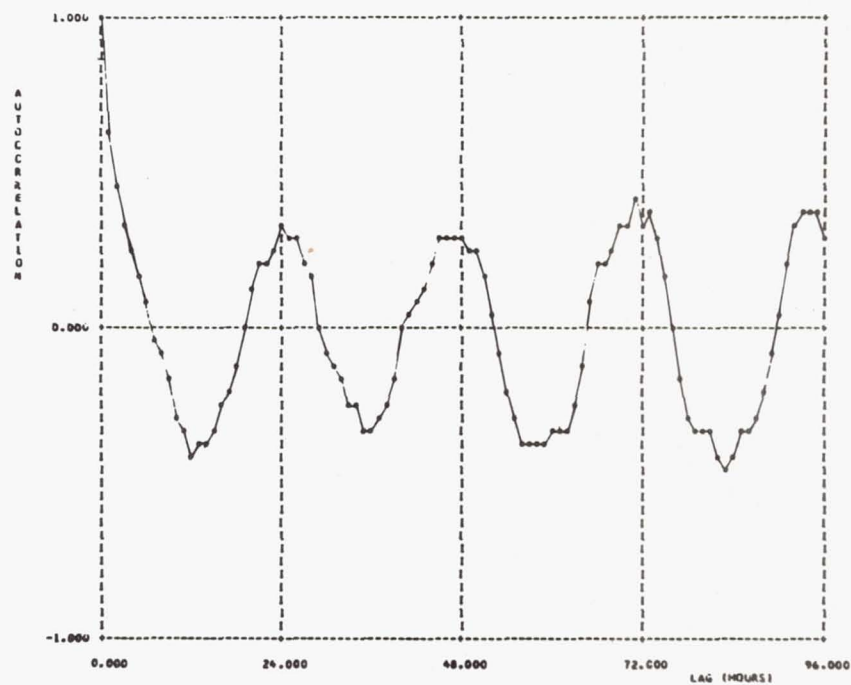
Figure 5. - Autocorrelation of body temperature for subject A during
8 days of the 23.5-hour lighting schedule.
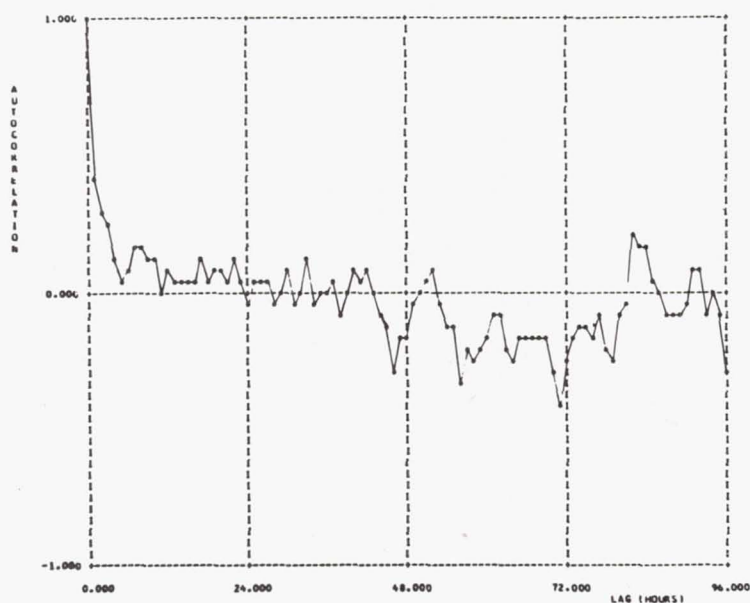
Figure 6. - Autocorrelation of body temperature for subject A during
first 6 days of constant light.
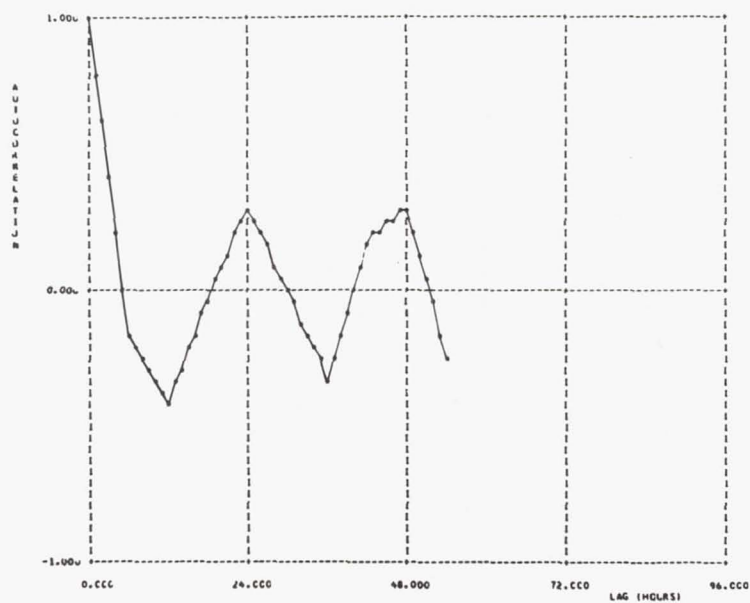
Figure 7. - Autocorrelation of urine 17-OH corticosteroids for subject A
during 8 days of 23.5-lighting schedule.
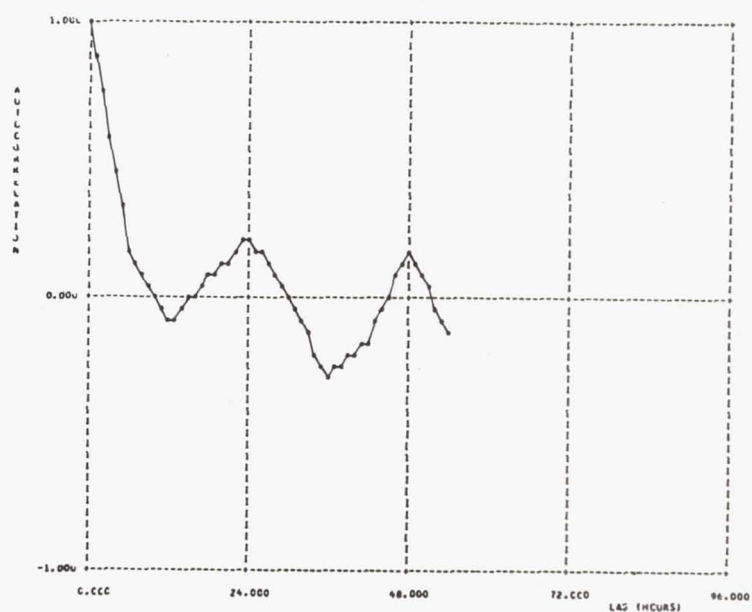
Figure 8. - Autocorrelation of urine 17-OH corticosteroids during
6 days of constant light.
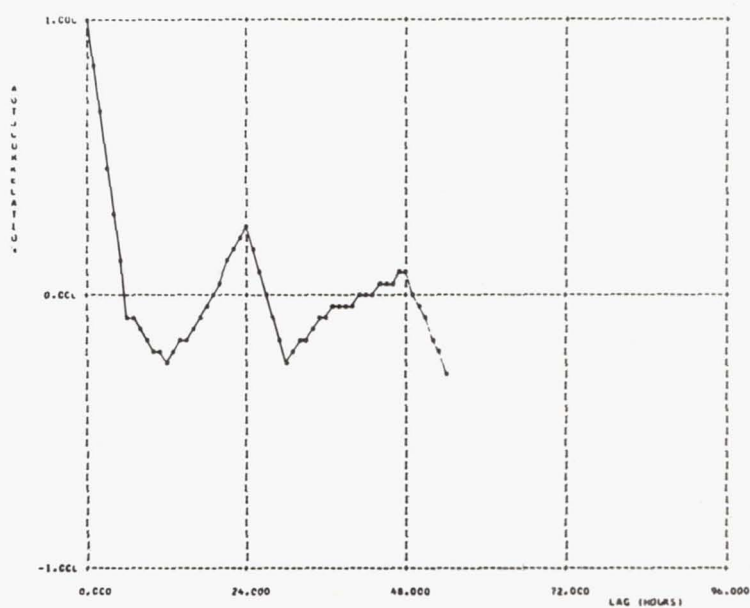
Figure 9. - Autocorrelation of urine potassium during
8 days of 23.5-hour lighting schedule.

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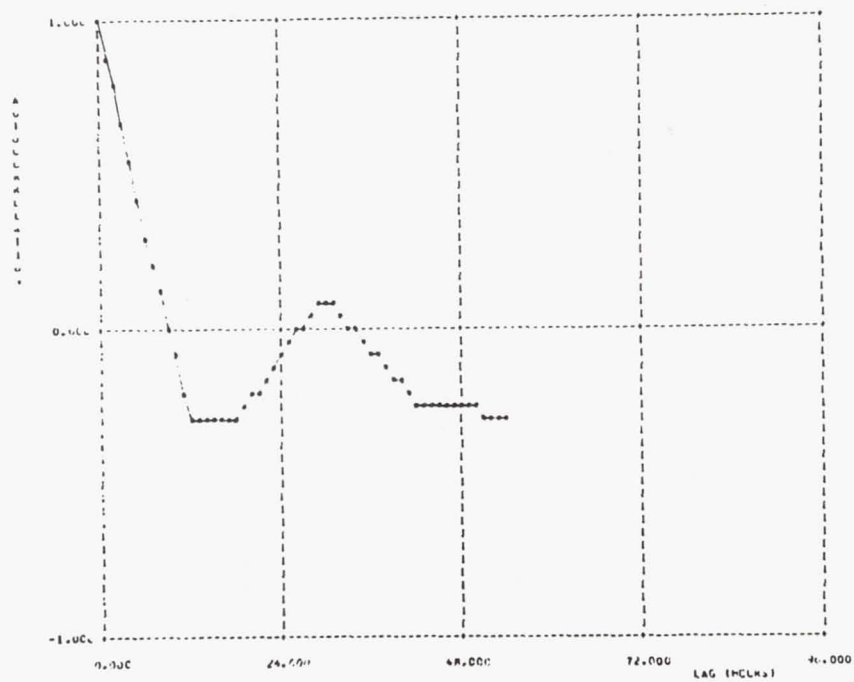
Figure 10. – Autocorrelation of urine potassium during
6 days of constant light.
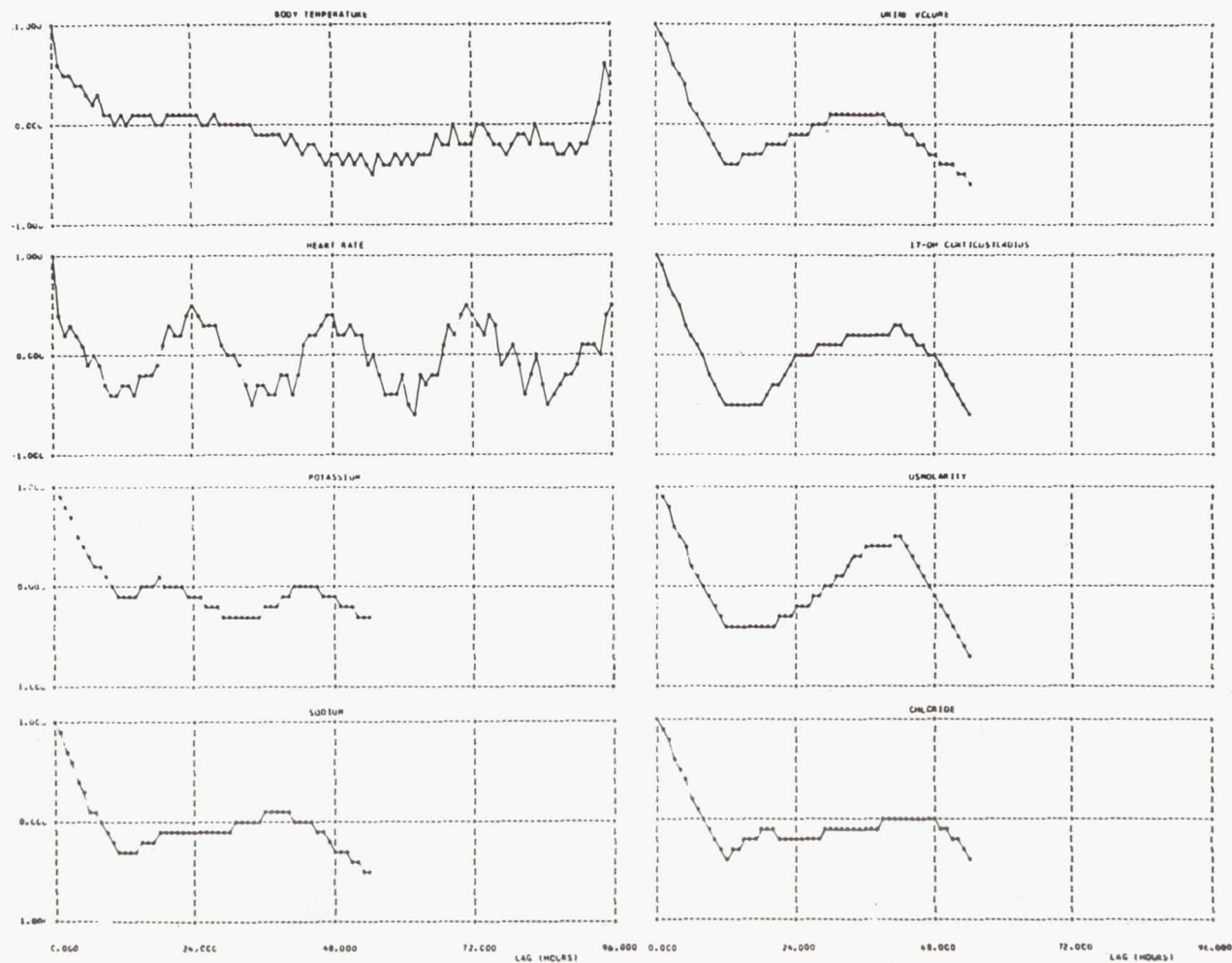
Figure 11. - Autocorrelation of all variables for subject A during first 5 days of adaptation period.
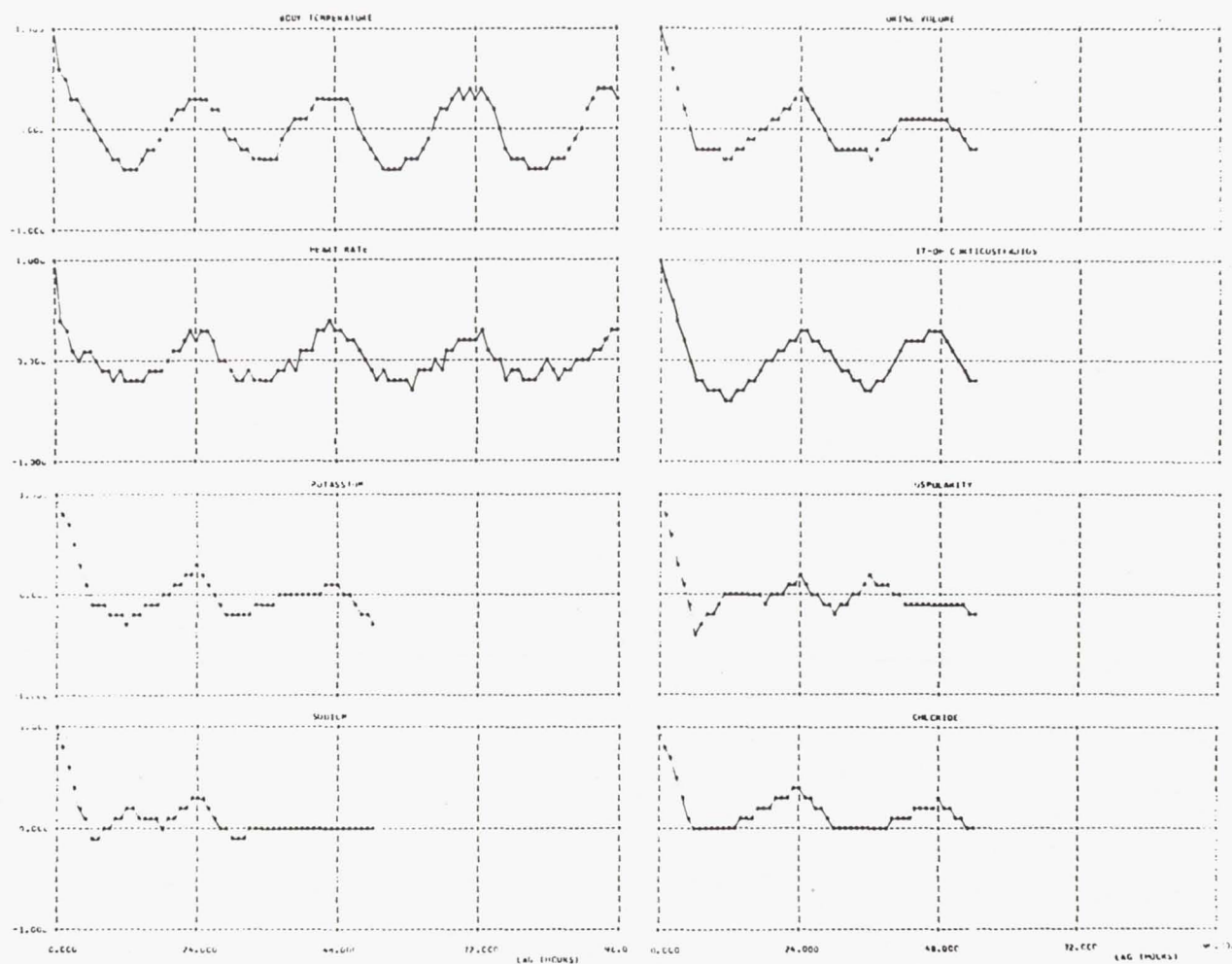
Figure 12. - Autocorrelation of all variables for subject A during 8 days of the 23.5-hour lighting schedule.

DISCUSSION

In looking at human circadian rhythms from three different view points we see that there is variability first of all between individuals. Also evident is the variable response of different human circadian rhythms to different environmental conditions. This produces the variable circadian homeostasis, which was noted in single individuals. The task now is to correlate the performance of individuals within the framework of these various types of circadian dysrhythmia.

The quantitative measurement of performance is at many times difficult. We found this particularly true with regard to motivation during the 30-day experiment. Although the results of the performance experiments will be given in a separate report, at this time we would propose that performance differences and trends were noted between individuals and during changes of the circadian makeup of single individuals. These will be investigated in greater detail during the more rigorous simulated Apollo mission experiments in which we are now engaged.

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EFFECTS OF TRANSITORY BEHAVIOR STRESS ON URINARY

17-HYDROXYCORTICOSTEROID AND CATECHOLAMINE LEVELS

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One of the more common observations resulting from laboratory analyses of astronaut blood and urine samples taken after the termination of projects Mercury and Gemini flights was an elevation in adrenal hormone concentrations. Figure 1 presents an example of this finding. A plasma sample taken less than 1 hour after reentry was compared with other samples, including a sample following a 5-mile run and with a calculation of the same individual's characteristic circadian variability in 17-hydroxycorticosteroid levels under basal conditions. It is interesting to note that the first postflight sample displayed 17-hydroxycorticosteroid (17-OH-CS) concentrations, which exceeded the physical stressor effect induced by the 5-mile run. The source of these changes in adrenal hormone concentrations has not been precisely identified, in the absence of sufficient urine sampling during or after flights. While the spacecraft environment introduces a variety of uncontrolled conditions that may interact to induce changes in adrenal activity, it is possible that this adrenal mobilization can be largely related to emotional variables. It probably represents a very normal set of adaptive mechanisms that are automatically set into operation when an individual is placed in environments requiring unusual demands upon performance. However, in view of the importance of the adrenal hormones for intact organismic functioning, it may be important to determine whether these adrenal hormone elevations adapt out as a function of time spent in the spacecraft environment. It is possible that these changes are specifically induced by the critical events associated with lift-off and reentry. If this is not so, and substantial degrees of adrenal mobilization are observed for long continuous periods of a flight, then the implications are more serious. Failure in pituitary-adrenocortical acclimatization to spacecraft environments could indicate the development of somatic pathology described previously by Selye as the "diseases of adaptation." The basic observation underlying the work of Selye is that continued compensatory efforts of the organism and of the pituitary-adrenocortical system in particular are responsible for development of specific disease processes upon continued exposure to stressful environment (1946).

MERCURY BIOCHEMICAL DATA
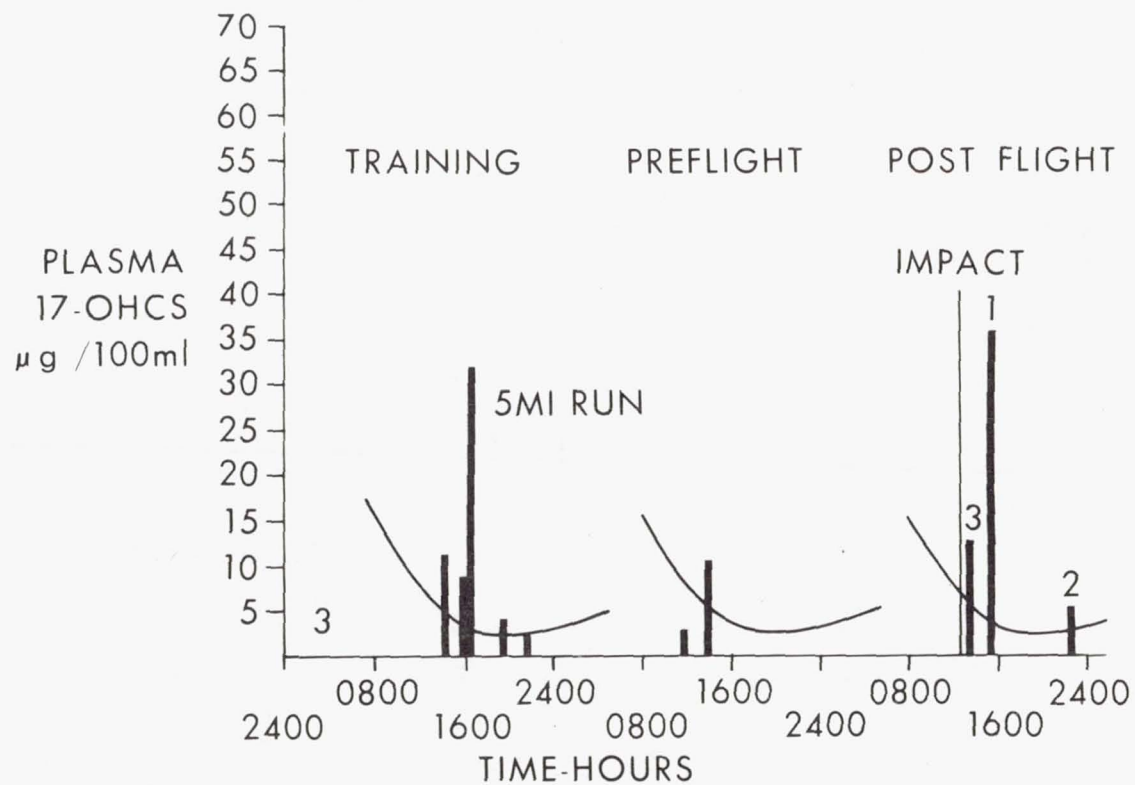
NASA-MSC W DIETLEIN 27 AUG 63 S-280-63

Figure 1

Others such as Ingle (1956) suggest that adrenal mobilization is involved, but not of etiological significance, in induction of these diseases.

As the manned space program progresses, this issue of adrenal mobilization should be resolved through analyses of inflight data. However, inflight data are accumulated very slowly and with certain unavoidable constraints which increase error variability. Moreover, adequate research foundations regarding this issue from the standpoint of laboratory stress research with humans have to be provided. In recognition of the latter problem, the Manned Spacecraft Center has supported a psychophysiological stress program by the present investigator. The present study is one of the more recent investigations resulting from this in-house program.

The goals of this specific study were to study the time course of elevations in the urinary excretion of 17-hydroxycorticosteroids, epinephrine, and norepinephrine, induced as by-products of transient behavior stress, and to relate these adrenal changes to changes in heart rate, pulse pressure, skin resistance, and to changes in three behavioral measures associated with alertness or vigilance. A stressor technique, developed through previous experiments of the psychophysiological stress program, was employed. With this technique, individuals were conditioned through discriminative avoidance conditioning procedures to undergo marked emotional changes during subsequent exposures to a previously neutral stimulus. In this case the conditional aversive stimulus was a light, which assumed aversive properties during a training trial through association with contingent electric shock punishment. The results obtained on the test trial, therefore, represent conditioned emotional responses, which occurred in the absence of actual punishment.

Definition of Behavior Stress

Before the method and results are discussed, the term "behavior stress" should be defined. Induction of behavior stress, as it has been conceptualized in the present program, requires three conditions. These conditions are: requiring the organism to perform near or beyond capacity limits, where performance failures lead to punishment, and where escape from the immediate environment is difficult or impossible. Each of these conditions is necessary, but insufficient alone to induce behavior stress. In the discriminative avoidance variation of the technique, which will be described in more detail, these conditions are met since a neutral stimulus achieves aversive properties through continuity with electric shock punishment during training. The

present difinition of behavior stress is not intended to be considered applicable to all stress situations in some universal sense. It is, however, useful for effective induction and study of emotional disturbances in the laboratory and it can be operationally specified.

METHOD

Stress Induction Procedure

The specific procedure for stress induction required human test subjects to monitor an instrument panel containing three voltmeters and detect pointer deflections. The meter faces were covered with one-way or silvered glass so that it was necessary to depress an observing key to illuminate the meter face. One observing key was provided for each meter. A 0.1-second flash duration was used for each observing key. When the subject detected a pointer deflection, he was required to reset the pointer to the original null position through depressing a detection lever corresponding to the same meter. If a detection was not made within a 3.0-second period from initial deflection, the pointer reset automatically. A 1.0-minute variable-interval signal presentation program was used to control pointer deflections in such a way that signal presentation sequence was randomized from one meter to another and so that intersignal intervals were variable. A small visual indicator light was on the instrument panel. This light was switched on and off periodically at 15-minute intervals during each of the three trials. During the training trial, the presence of the light indicated that punishment was available when signals were not detected. Electric shock was used as the punishing agent. Shock was dispensed through 2 cm^2 electrodes located across the calf of the left leg. The shock stimulus was set at a 150-millisecond duration with an ac current of $6.5 \text{ milli amp/cm}^2$ of electrode surface area. A paste was used which was isotonic to normal skin perspiration and shock electrode sites were prepared through skin abrasion to eliminate variations in skin resistance.

Subjects

Ten healthy males between 17 and 27 years of age were employed as experimental subjects and the mean age of the group was 20.7 years. Each subject was given sufficient practice in the task prior to data collection to insure that the task was learned. Prior to the training trial subjects were instructed in the nature of the contingency between

signal detection and shock avoidance to eliminate unnecessary punishments. They were also told at this time that punishment was available only when the visual stimulus was on. The baseline periods which intervened were "safe" periods, although the subject was still to perform as well as possible for each period of each trial.

Apparatus

The behavioral control and recording equipment included commercially available timers, relays, printout counters, and cumulative recorders. Probability of signal detection was calculated from printout counter records. Signal detections, shocks, and observing responses were also recorded on a cumulative recorder.

Heart rate was measured through amplifying and preprocessing EKG signals to operate a relay which, in turn, operated a printout counter. Blood pressure was recorded through the use of an automatic cuff pump, a crystal microphone, and an Offner 8-channel recorder. Exosomatic skin resistance was recorded using a constant current dc voltage to provide a 6.5μ amp/cm^2 current density.

Subjects were placed during the trial in a small sound attenuated chamber containing the instrument panel and a recliner chair. Visual observation of subjects was permitted through one-way glass ports and a communications system permitted monitoring of subject comments during the trial. After a trial began, there was no verbal interchange between experimenter and the subject until trial termination.

Experimental Procedure

The procedure used in the present experiment required testing each subject for 4 consecutive days. The first day was used for habituation to the test environment and no behavioral or physiological data were taken. The second day was used to obtain control data on each measure employed. The third day was used for conditioning subjects. The fourth day was used as the test day. The only difference in experimental procedure from day 2 through day 4 was the use of electric shock on the training trial during periods signified by the visual discriminative stimulus (S^d). Procedures on day 2 and day 4 were identical. Consequently, the effectiveness with which changes were induced on day 4 depended upon the degree that the previously neutral visual stimulus had achieved conditioned adversive properties through training on day 3.

Each day began with an initial urination at 8:30 a.m. The first
sample on each day was taken at 10:30, immediately before the subject
began to perform the monitoring task. At 12:15, the monitoring task
was terminated and the second urine sample was taken. The third urine
sample was taken at 2:15 p.m. and the fourth sample was taken at 4:15 p.m.
A fifth sample was taken at 6:15 p.m. Epinephrine and norepinephrine
samples were acidified with H_2SO_4 and frozen. Samples for 17-OH-CS
analysis were frozen without adding preservatives. Subjects rested in
an isolated house trailer when they were not working in the experimental
chamber. Catecholamine determinations were performed using the Weil-
Malherbe and Bone method (1957). The 17-hydroxycorticosteroid determin-
ations were performed with the Peterson and Wyngaarden method (1955).

RESULTS

Behavioral Results

Figure 2 presents group epoch (period) means for the ten subjects
representing performance data on each trial. Epoch duration was 15 min-
utes. The visual stimulus, therefore, was presented for three 15-minute
periods per trial, alternating with four baseline epochs when the stim-
ulus was off. On the control day, there was very little interepoch
variation within measures. There was, however, a consistently increas-
ing trend in observing rates and signal detection, correlated with a
decreasing trend in response latency. On the conditioning day, when
electric shock was available in the presence of the visual stimulus,
behavioral baselines again showed the increasing trend but superimposed
upon this trend were marked interepoch variations with increased ob-
serving rates and signal detection and with decreased response latencies
during avoidance epochs. On the test day, the light alone induced the
same fluctuations with even greater differences from control values than
those observed during training. Statistical analyses of the behavioral
data led to the following conclusions: the visual stimulus was a neu-
tral stimulus prior to training; control trial-test trial differences,
comparing across S^d epochs, were highly significant; there was a gen-
eralized increase in baseline epoch values during the test trial over
control baseline periods; and, significant differences were obtained
between baseline and experimental (S^d), epochs within the test trial.
The t-test results obtained from testing will be presented elsewhere.

Figure 3 presents group epoch means for heart rate, blood pressure,
and log skin resistance for the same trials. Again, results of t-tests

PERFORMANCE RESULTS FOR TEN
SUBJECTS TESTED FOR THREE TRIALS,
WITH FOUR BASELINE AND THREE
DISCRIMINATIVE STIMULUS
EPOCHS PER TRIAL
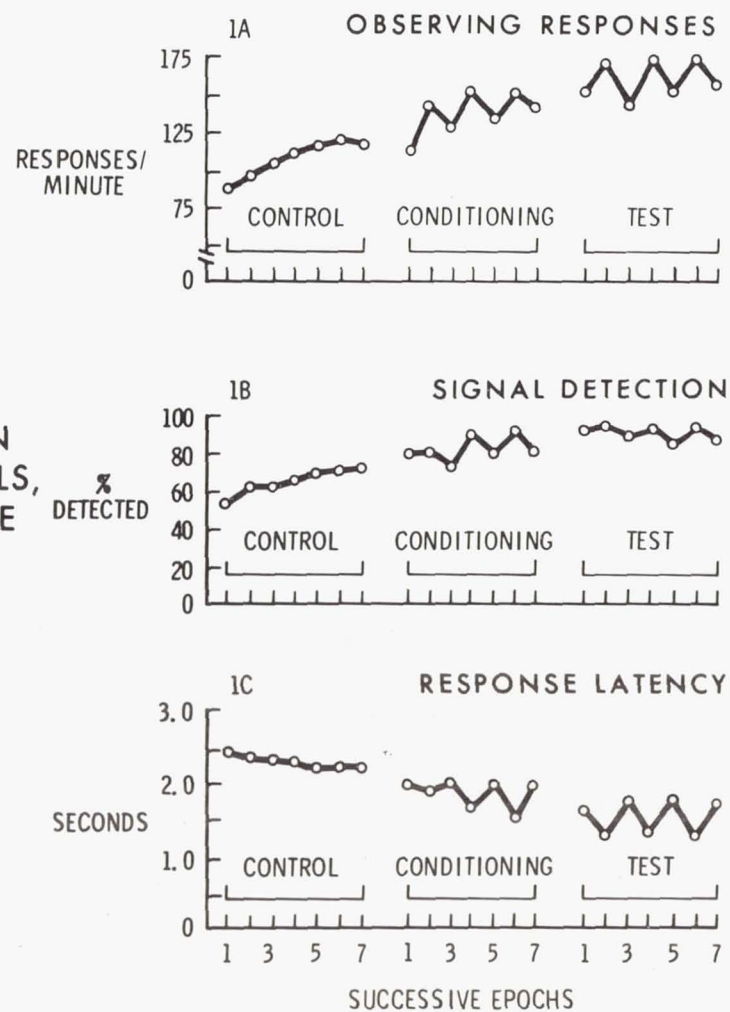
Figure 2

PHYSIOLOGICAL RESULTS FOR TEN
SUBJECTS TESTED FOR THREE
TRIALS WITH FOUR BASELINE
AND THREE DISCRIMINATIVE
STIMULUS EPOCHS PER TRIAL
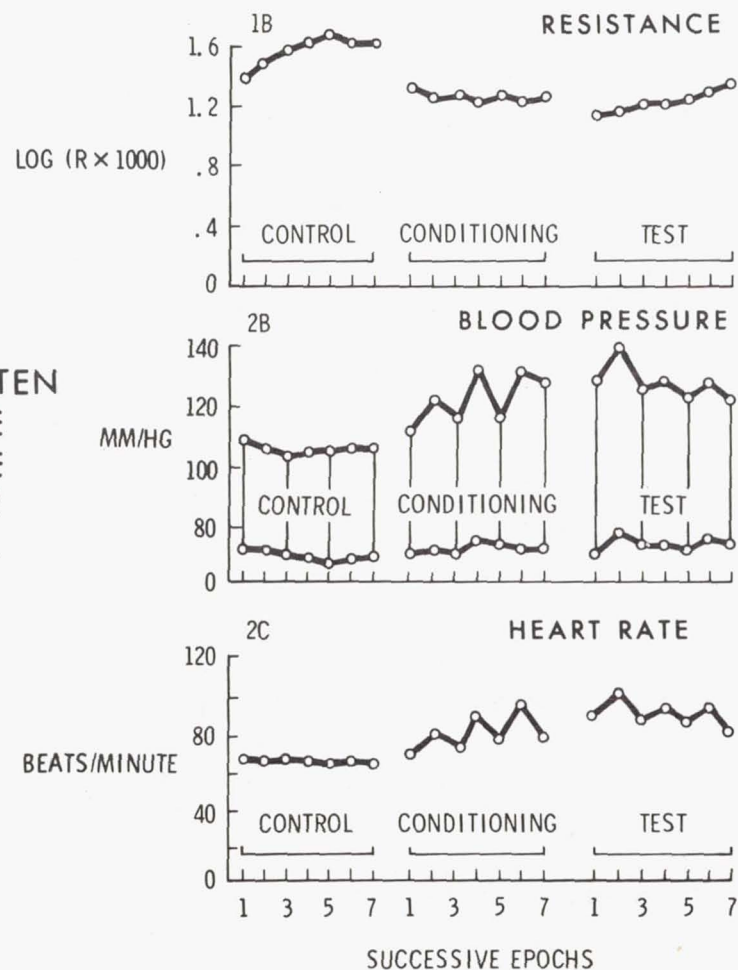
Figure 3

for correlated data revealed that the light was a neutral stimulus during the control trial in baseline-experimental epoch comparisons. Significant increases in heart rate and pulse pressure and decreases in resistance were found in comparing experimental epochs between control and test trials for each physiological measure. In comparing experimental and baseline epochs within the test day, significant differences were found both for heart rate and pulse pressure but not for skin resistance, which appeared to maintain extremely low values throughout the test trial for most subjects. It seems most likely that resistance tended to reach minimal limits for these individuals during baseline epochs of the test trial and was, therefore, unable to decrease further as arousal was further increased by the light. These results will also be described in more detail elsewhere.

Biochemical Results

In view of the rather clear behavioral and autonomic nervous system evidence of success in inducing behavior stress, it seemed rather likely that significant changes would be noted in the adrenal hormone measurements. It was not known, however, when peak excretion rates would be observed nor how persistant adrenal changes would be.

Figure 4 presents group mean excretion rates for 17-OH-CS, epinephrine, and norepinephrine. While the 17-OH-CS data are based upon the entire group of ten subjects, the epinephrine and norepinephrine data from one subject were contaminated by tetracycline medication which led to spurious flourescence regardless of laboratory efforts to eliminate these effects. Consequently, these data were not included in the statistical data analysis. It is noted in inspecting the 17-OH-CS data, that apparent elevations incurred immediately after the training trial and in the sample taken 2 hours later. On the test day, there was a clear elevation in 17-OH-CS excretion in the sample collected immediately after the test trial. Epinephrine group means followed a very similar trend, with elevations at the same points in time. The first sample of the test day also showed an epinephrine elevation above the corresponding control value which was not shared by the other two hormones. The norepinephrine means displayed a clear elevation in the sample taken immediately after the trial on the test day. On the conditioning day, elevations above control values were observed for each sample except the sample taken immediately after the trial. The reason for this discrepancy is unknown.

Table I presents results of t-tests of training-trial-control trial differences for 17-OH-CS. A significant difference (p < .025) was found between the sample taken immediately following the training trial
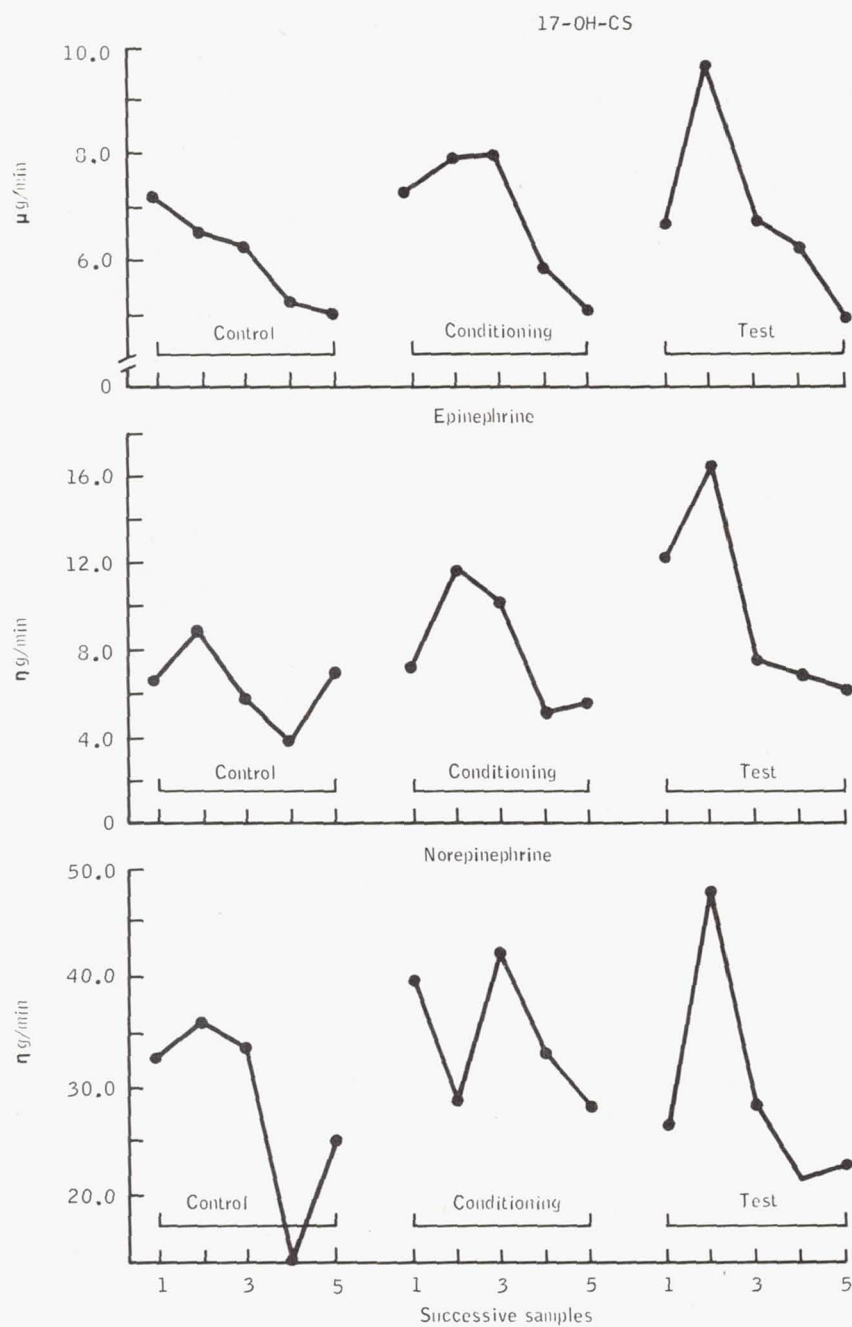
17-OH-CS

Figure 4

RESULTS OF t-TESTS OF DIFFERENCES BETWEEN CONTROL AND TRAINING DAYS IN 17-OH-CS EXCRETION RATES FOR TEN SUBJECTS

PERIOD	MEAN CONTROL	MEAN TRAINING	S_{DIF}	t
8:30 - 10:30	6. 87	7. 27	0. 922	0. 44
10:30 - 12:15	6. 52	7. 83	0. 504	2. 61*
12:15 - 2:15	6. 24	7. 89	0. 966	1. 71
2:15 - 4:15	5. 18	5. 83	1. 011	1. 27
4:15 - 6:15	4. 94	5. 05	0. 502	0. 22
8:30 - 6:15 (OVERALL)	6. 01	6. 76	0. 451	1. 44

*SIGNIFICANT AT .025 LEVEL

Table I

and the comparable sample following the control trial. While the group
mean of the sample taken 2 hours later on the training trial was actu-
ally higher, the t value obtained in comparing this sample with the
comparable sample on the control day only approached significance
(p < .10). It is interesting to note that the differences between the
overall means for the control and training days were insignificant,
illustrating the transient nature of the 17-OH-CS change.

Table II presents results of the same tests for evaluating differ-
ences between the control and test days for 17-OH-CS excretion. Again,
a highly significant difference (p < .005) was found for the sample
taken immediately after the test trial.

Further comparisons were made between the samples taken on the
test day, between the sample of primary interest and each of the other
samples. Table III indicates that the sample taken immediately after
trial termination showed a significantly higher excretion rate of
17-OH-CS than any other sample obtained on the test day.

The statistical analyses for epinephrine excretion rates revealed
similar elevations on the test day but there were several differences
in results of the other epinephrine analyses. Table IV presents re-
sults of t-tests performed to evaluate differences between comparable
samples on the conditioning and control days. The magnitude of these
differences failed to reach a significant level for any sample of the
training trial. However, comparisons between control and experimental
day samples, summarized in Table V, revealed significant differences in
the expected directions, both for the pre-test sample (p < .05) and for
the sample taken immediately after the trial (p < .05). In addition,
the differences between the overall or combined samples for the control
and test days were significant for epinephrine (p < .05), as indicated
in Table V. When the second sample of the test day was compared with
the other samples on the same day, significant differences were obtained
for all comparisons except the comparison between the first or pre-test
sample, and the second sample. Table VI presents these results.

The epinephrine results, therefore, show a transient elevation on
the test day, which was attributable to intermittent presentations of
the visual stimulus alone. It seems likely that the elevation in the
first sample of the test day might be attributed only to an anticipation
or "test anxiety" phenomenon which was not apparent in the other hor-
monal measures.

While the urinary norepinephrine data analyses also revealed a
significant transient elevation of the test day, consistent with 17-OH-CS
and epinephrine results, they failed to reveal a similar elevation on

RESULTS OF t-TESTS OF DIFFERENCES BETWEEN CONTROL AND EXPERIMENTAL DAYS IN 17-OH-CS EXCRETION RATES FOR TEN SUBJECTS

PERIOD	$\bar{X}_c$	$\bar{X}_e$	$\bar{d}$	$S_{\bar{d}}$	$t_{\bar{d}}$	p
8:30 - 10:30	7.15	6.67	-0.48	0.811	0.591	N.S.
10:30 - 12:15	6.52	9.65	3.14	0.612	5.12	.005 *
12:15 - 2:15	6.24	6.68	0.44	1.030	0.43	N.S.
2:15 - 4:15	5.18	6.21	1.03	1.724	0.60	N.S.
4:15 - 6:15	5.02	4.88	-0.14	0.483	0.30	N.S.
8:30 - 6:15 (OVERALL)	6.01	6.93	0.93	0.566	1.64	N.S.

* ONE-TAILED TEST IN THIS CASE

Table II

RESULTS OF t-TESTS OF 17-HYDROXYCORTICOSTEROID EXCRETION COMPARING DIFFERENCES BETWEEN THE FIRST POST-TEST SAMPLE WITH THE OTHER SAMPLES TAKEN ON THE TEST DAY

COMPARISON	SAMPLE 2 MEAN	COMPARISON SAMPLE MEAN	$S_{d\bar{d}}$	t^t
SAMPLE 2 - SAMPLE 1	9.65	6.67	1.01	2.92*
SAMPLE 2 - SAMPLE 3	9.65	6.68	1.35	2.28**
SAMPLE 2 - SAMPLE 4	9.65	6.21	1.05	3.38***
SAMPLE 2 - SAMPLE 5	9.65	4.88	1.37	2.60*

*SIGNIFICANT AT .025 LEVEL

**SIGNIFICANT AT .01 LEVEL

***SIGNIFICANT AT .005 LEVEL

Table III

RESULTS OF t-TESTS OF DIFFERENCES BETWEEN CONTROL AND TRAINING DAYS IN EPINEPHRINE EXCRETION RATES FOR NINE SUBJECTS

PERIOD	MEAN CONTROL	MEAN TRAINING	S_{dif}	t
8:30 - 10:30	6.62	7.08	1.04	0.09
10:30 - 12:15	8.79	11.76	2.12	0.69
12:15 - 2:15	5.88	10.11	2.19	0.62
2:15 - 4:15	3.76	5.13	3.80	1.37
4:15 - 6:15	6.98	5.52	3.24	0.92
8:30 - 6:15 (OVERALL)	6.24	7.90	1.16	1.43

Table IV

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RESULTS OF t-TESTS OF DIFFERENCES BETWEEN CONTROL AND EXPERIMENTAL DAYS IN EPINEPHRINE EXCRETION RATES FOR NINE SUBJECTS

PERIOD	MEAN CONTROL	MEAN EXPERIMENTAL	S_{dif}	t
8:30 - 10:30	6.62	12.32	2.42	1.89*
10:30 - 12:15	8.79	16.49	4.05	1.90*
12:15 - 2:15	5.88	7.51	3.17	0.68
2:15 - 4:15	3.76	6.82	2.25	1.25
4:15 - 6:15	6.98	6.14	1.42	0.66
8:30 - 6:16 (OVERALL)	6.24	9.90	1.84	1.98*

*SIGNIFICANT AT .05 LEVEL

Table V

RESULTS OF t-TESTS OF EPINEPHRINE EXCRETION COMPARING DIFFERENCES BETWEEN THE FIRST POST-TEST SAMPLE AND THE OTHER SAMPLES TAKEN ON THE TEST DAY

COMPARISON	SAMPLE 2 MEAN	COMPARISON SAMPLE MEAN	S_d	t
SAMPLE 2 - SAMPLE 1	16. 49	12. 32	5. 40	0. 77
SAMPLE 2 - SAMPLE 3	16. 49	7. 51	4. 50	2. 00*
SAMPLE 2 - SAMPLE 4	16. 49	6. 82	4. 70	2. 16*
SAMPLE 2 - SAMPLE 5	16. 49	6. 14	5. 04	2. 01*

* SIGNIFICANT AT . 05 LEVEL

Table VI

the conditioning day. Table VII presents results of t-tests performed
to assess training trial-control trial differences in norepinephrine
for comparable samples. It will be noted that a significant difference
was detected for the comparison between the fourth sample of the train-
ing and control days. The reason is clearly not attributable to an
increase in norepinephrine excretion during the training day, but to an
unusual reduction in norepinephrine on the control day for the corre-
sponding sample. When this reduction occurred is unclear.

Table VIII presents results of control day-test comparisons for
norepinephrine. Here the significant difference between the sample
taken immediately after the trial and the comparable control sample
was clearly attributable to an elevation on the test day. In comparing
this sample with the other samples taken on the test day, significant
differences were obtained in two out of four comparisons, and a third
comparison was virtually significant (t = 1.88), as indicated in
table IX.

In conclusion, each of the three adrenal hormones displayed a sig-
nificant elevation in the urine samples taken immediately following the
test trial. Moreover, there was a rather clear similarity of group
trends between cortical and medullary hormones, particularly in com-
paring 17-OH-CS and epinephrine excretion, suggesting close relation-
ships in activation patterns in situations involving intermittent high-
level stress imposed over short periods.

CORRELATION ANALYSES

In calculating product-moment correlation coefficients, comparisons
were obtained through calculating differences between the second sample
on the test day and the second sample on the control day for each of
the three hormonal measures. In correlating the hormonal differences
between the control trial and test trial sample with the behavioral and
physiological measures, baseline and avoidance epoch data were combined
for the physiological and behavioral measures to give an integrated or
overall trial estimate both for the control trial and for the experi-
mental trial. Different scores were calculated for each subject from
these overall trial values for correlation with the hormonal differences.

17-Hydroxycorticosteroid Correlations

Table X presents a correlation matrix based upon control trial-test
trial differences for each of the measures used in the study. Inter-
correlations involving catecholamines are based upon a sample of nine,
while all other correlations are based upon an N of 10.

RESULTS OF t-TESTS OF NOREPINEPHRINE EXCRETION COMPARED BETWEEN TRAINING AND CONTROL TRIALS (N=9)

PERIOD	MEAN TRAINING	MEAN CONTROL	S_d	t
8:30 – 10:30	39. 92	32. 94	6. 13	1. 14
10:30 – 12:15	28. 52	36. 22	6. 82	1. 13
12:15 – 2:15	42. 22	33. 81	23. 76	0. 51
2:15 – 4:15	33. 08	13. 95	9. 26	2. 07 *
4:15 – 6:15	28. 10	25. 12	7. 32	0. 48
8:30 – 6:15 (OVERALL)	33. 90	27. 91	4. 91	1. 22

*SIGNIFICANT AT .05 LEVEL

Table VII

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RESULTS OF t-TESTS OF NOREPINEPHRINE EXCRETION COMPARED BETWEEN TEST AND CONTROL TRIALS (N=9)

PERIOD	MEAN TEST	MEAN CONTROL	S_d	t
8:30 - 10:30	26. 52	32. 94	6. 70	0. 96
10:30 - 12:15	47. 28	36. 22	5. 20	1. 87 *
12:15 - 2:15	28. 22	33. 81	4. 60	0. 80
2:15 - 4:16	21. 49	13. 95	6. 32	1. 18
4:15 - 6:15	22. 84	25. 12	3. 60	0. 29
8:30 - 6:15 (OVERALL)	29. 94	27. 91	2. 17	0. 99

*SIGNIFICANT AT .05 LEVEL

Table VIII

RESULTS OF t-TESTS OF NOREPINEPHRINE EXCRETION COMPARING DIFFERENCES BETWEEN THE FIRST POST-TEST SAMPLE AND THE OTHER SAMPLES TAKEN ON THE TEST DAY

COMPARISON	SAMPLE 2 MEAN	COMPARISON SAMPLE MEAN	$S_{\bar{d}}$	t
SAMPLE 2 - SAMPLE 1	47.28	26.52	10.87	1.91*
SAMPLE 2 - SAMPLE 3	47.28	28.22	8.87	2.15*
SAMPLE 2 - SAMPLE 4	47.28	21.49	13.38	1.88
SAMPLE 2 - SAMPLE 5	47.28	22.84	9.88	1.63

*SIGNIFICANT AT .05 LEVEL

Table IX

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PRODUCT-MOMENT CORRELATIONS BETWEEN ABSOLUTE
CHANGES ABOVE CONTROL TRIAL LEVELS FOR PAIRS OF
MEASURES TAKEN DURING THE TEST TRIAL

MEASURE	17-OH-CS	EPINEPHRINE	NOREPINEPHRINE
SKIN RESISTANCE	.056	-.459	-.294
PULSE PRESSURE	.827***	-.168	.562*
HEART RATE	.399	.346	-.112
RESPONSE LATENCY	-.456	-.460	-.509
SIGNAL DETECTION	.531*	.565*	.814***
OBSERVING RATE	.238	.317	-.201
NOREPINEPHRINE	.463	.451	---
EPINEPHRINE	.451	---	
17-OH-CS	---		

* SIGNIFICANT AT .05 LEVEL

*** SIGNIFICANT AT .005 LEVEL

Table X

From the standpoint of the pituitary adrenocortical system, the highest correlation was obtained between 17-OH-CS change and pulse pressure change ($r = .83$). This correlation is significant at the .005 level. The second significant correlation coefficient involving 17-OH-CS was obtained from the comparison with change in probability of signal detection. This coefficient of .57 was significant at the .05 level.

It is interesting to note that the 17-OH-CS pulse pressure relationship was much higher than correlation coefficients between pulse pressure and the catecholamines. While it has been established that intact adrenocortical functioning is necessary to maintain blood pressure and that 17-OH-CS release plays several permissive or indirect roles in increasing blood pressure, this finding was not consistent with expectations based on the general literature.

The finding of a significant relationship between 17-OH-CS changes and signal detection suggests closer relationships between 17-OH-CS release and changes in performance effectiveness than between 17-OH-CS release and rate of response or response speed. It is tempting to suggest that the organism increases performance effectiveness in avoidance situations to maximal or near maximal limits only at some cost to the adrenal gland. In other words, 17-OH-CS elevation may be considered as a hormonal correlate of high fear motivation. In earlier studies of the psychophysiological stress program it was theorized that one effect of superimposing an avoidance contingency upon the monitoring task was an increase in the reinforcement value of signal detection. Consequently, this finding of a significant 17-OH-CS-signal detection relationship might be interpreted as consistent with this previous hypothesis.

Epinephrine Correlations

Table X presents correlations between epinepnrine and the other measures employed. Again, a significant correlation was found between epinephrine changes and signal detection ($r = .56$), suggesting again that probability of signal detection is a critical behavioral variable. Perhaps the most remarkable feature of the epinephrine correlations was the lack of correspondence between epinephrine and pulse pressure and between epinephrine and heart rate. These two coefficients cast some doubt upon the advisability of using systolic or pulse pressure elevations in stress research as an index of epinephrine changes, because while epinephrine changes did occur, they were not significantly correlated with the pulse pressure or heart rate changes observed.

Norepinephrine Correlations

Norepinephrine correlations revealed a highly significant relation-
ship with signal detection. A correlation of .81 was found, which is
significant at the .005 level. A correlation of this magnitude is un-
usual in comparisons across life systems under any circumstances. This
finding is interpreted in much the same way as the other two adrenal
measures. The correlation between norepinephrine and pulse pressure
was significant (r = .56), but lower than the 17-OH-CS-pulse pressure
correlation coefficient value.

SUMMARY AND CONCLUSIONS

In summarizing the results and conclusions of the present experi-
ment, the conditioned stress induction procedure led to significant
changes in every measure studied. As a methodological demonstration,
the results indicate that conditioning techniques can provide a rather
powerful means for the study of emotional variables at various life
system levels. From the standpoint of adrenal temporal dynamics, the
results indicate that adrenocortical and medullary elevations are
found in urine immediately following brief periods of behavior stress,
but that these changes may not be detected if sampling periods are long
or if the subject urinates before the test sample is taken. While
17-OH-CS elevations were invariably found in the immediate aftermath of
conditioned stress, intercorrelation data indicated that norephrine
showed the highest relationship to signal detection. Higher correlations
were found between 17-OH-CS changes and pulse pressure than between
medullary activity and pulse pressure, suggesting that the practice of
using cardiovascular data alone to predict catecholamine trends may
lead to error.

In comparing the hormonal findings, it was found that simultaneous
changes did occur among the three measures, indicating similarities in
activation patterns in situations involving high-level stress imposed
over short periods. It seems not only possible, but likely, that this
adrenal medulla-pituitary-adrenocortical covariation would break down
in situations involving lower-level, but more sustained stress induction.
Future research comparing cortical and medullary activation patterns as
a function of interactions between stress level and stress duration
might provide very fruitful insights into the integration of organismic
adjustments to emotional stress, as well as a potential means for esti-
mating stress characteristics on the basis of observed relationships
between the catecholamines on the one hand, and glucocorticosteroids on
the other.

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THE INTERACTION OF ANGULAR ACCELERATION

AND HEAD TURNING VESTIBULAR FUNCTION

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A question of major concern during the 1965 Symposium on "The Role of Vestibular Organs in the Exploration of Space" was the applicability of data from simulators and vestibular studies performed in the lg earth environment to the situation of a rotating spacecraft in a null gravity condition. In the space situation, the position and alignment of the upright crewman are such that his spine is parallel with the centrifugal vector and in the plane of spin. Though it is possible to build a revolving space station simulator so that the resultant gravito-centrifugal vector is parallel to an upright subject's spine, within practical design it is not possible to have his spine simultaneously parallel to the spin plane.

In the rotating spacecraft situation, all motions of the head about the Z (spinal) axis when upright will be movements that are perpendicular to the plane of spin. Such movements will cause maximum labyrinthine Coriolis accelerations. In contrast, head movements about a Y (side-to-side) axis can vary from being in, to 90° out of, the plane of spacecraft spin. Loret has suggested that this orientation contrast may well dictate the placement of displays and controls in the artificial gravity spacecraft, but little effort has been made to quantitatively investigate this important concept. The requirement definitely exists for experimentation that will provide design engineers with normogravic data that can be reasonably extrapolated to spacecraft now being considered for long-term missions.

Gray collected observations from three subjects who were exposed to lg or 3g at a 50-foot radius while being rotated in a gimballed gondola at various angles to the centrifuge axis. The authors performed an excellent mathematical analysis of the possible effective torques which might have been generated in the subjects' semicircular canals by the cross-coupled rotations, but the data collected were not of an objective quantitative nature. Though it was statistically apparent that

the reported oculogyral illusions increased in those orientations expected to cause the greatest Coriolis accelerations in the semicircular canals, Gray cautioned that the otoliths were also being affected by different accelerations in the various maneuvers. In the space situation, in contrast, linear accelerations will maintain an essentially constant direction, providing a nearly constant stimulus to the otoliths, thus reducing the relevance of Gray's data to the construction of design envelopes.

Stone and Letko did a series of studies of men doing a simple task that required either turning the head (Z axis) and/or nodding the head (Y axis) while lying supine and being rotated in a centrifuge. In these studies, the spine was in the plane of spin, but not aligned with the resultant force. Both head motions were made 90° from the plane of spin, orientations where only maximum stimulation would be expected, whereas design constraints can only be derived from investigating the full stress range to be encountered during an activity. Paradoxically, the rapid recycling of the head turns in this study may have prevented all but a minimal cupular deflection to occur.

Loret suggested that the correlation between simulation on earth and the space situation might be defined if a simulator could be provided with a long enough centrifuge arm so that a tolerable spin rate would provide 1g radially, inclining the simulator floor at 45° from the g vector. Then by reclining a subject in a chair at 45° to the simulator floor it would be possible to position his Z axis in the plane of spin (with his head toward the spin axis), or at right angles to the plane of spin (with his feet toward the center of rotation). (See fig. 1.) In any position, his Z axis would always be displaced from the gravito-centrifugal resultant by 45°, providing a constant otolith stimulus in all head turn planes.

Our laboratory's Revolving Space Station Simulator (fig. 2) was capable of providing such an environment and the experiment was performed on a preliminary basis. Subjects were required to turn their heads through a 70° angle and immediately perform a psychomotor test (RATER, for Response Analysis Tester). The test results are shown on figure 3. A steady decrease in performance ability occurred as the angle between the plane of head rotation and the plane of simulator spin increased. This function agreed with earlier concepts about such an environment but did not provide enough information for design since it concerned only Z axis head movements.

AT 12.2 RPM MRSSS IS INCLINED AT 45°
FIGURES SHOW RELATION OF "PLANE OF HEAD TURN" TO PLANE OF SPIN
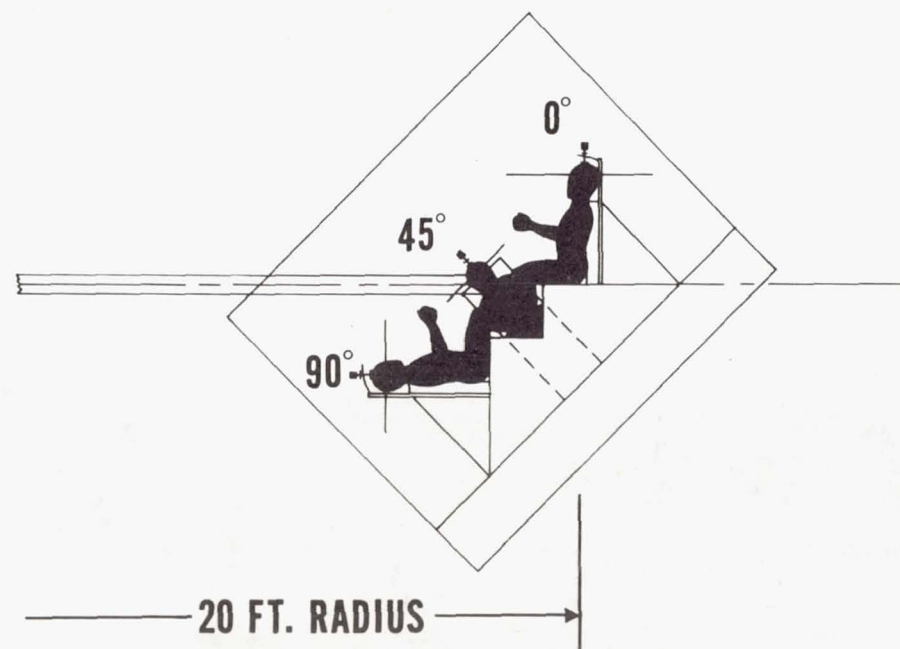
Figure 1. - Monaxial head turn: relation of planes of Z axis head turns to plane of manned revolving space station simulator (MRSSS) spin.
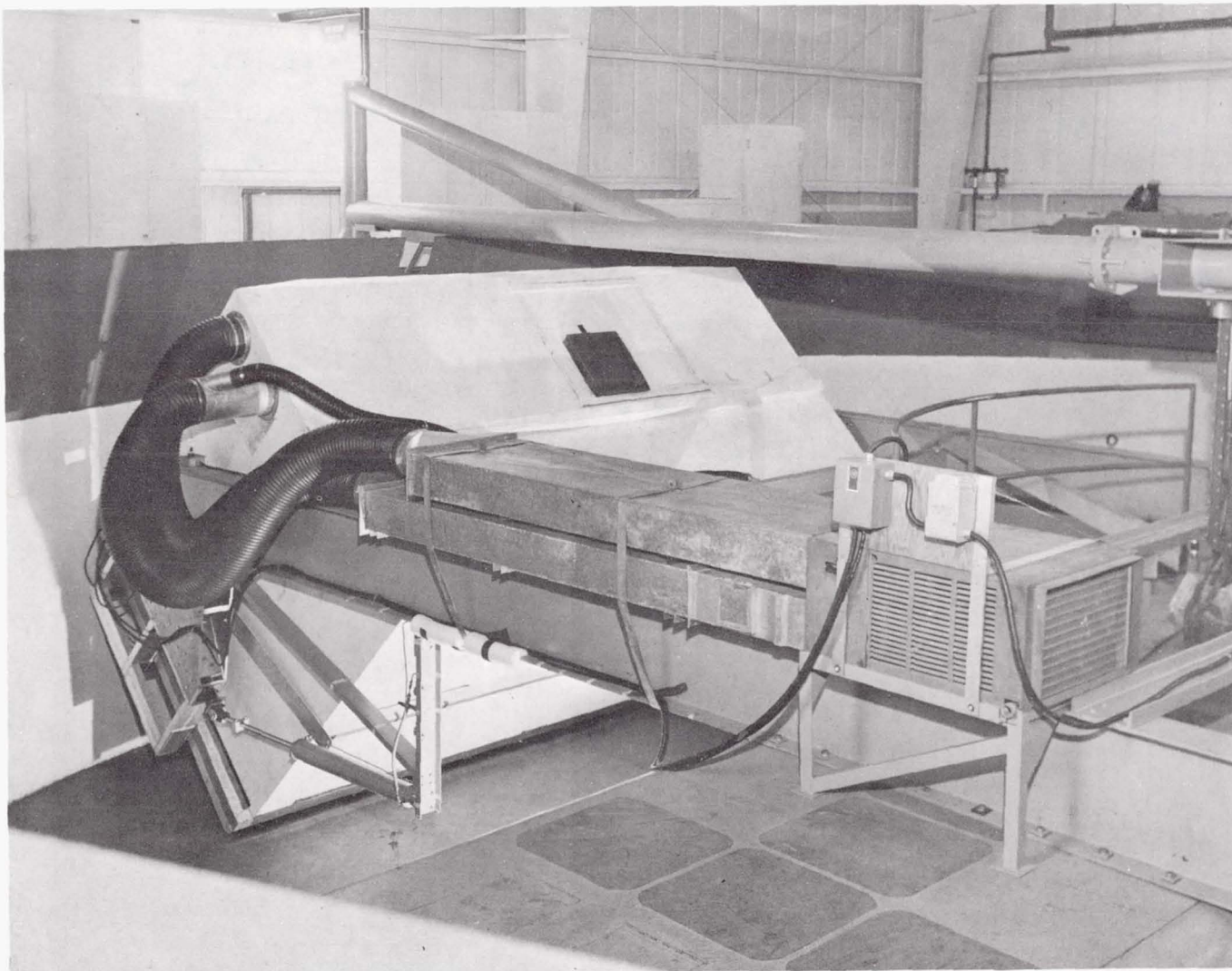
Figure 2. - MRSSS inclined at 45° while spinning at 12.2 rpm.

RATER PERFORMANCE FOLLOWING HEAD TURNS IN DIFFERENT PLANES AT 12.2 RPM & 45° INCLINATION
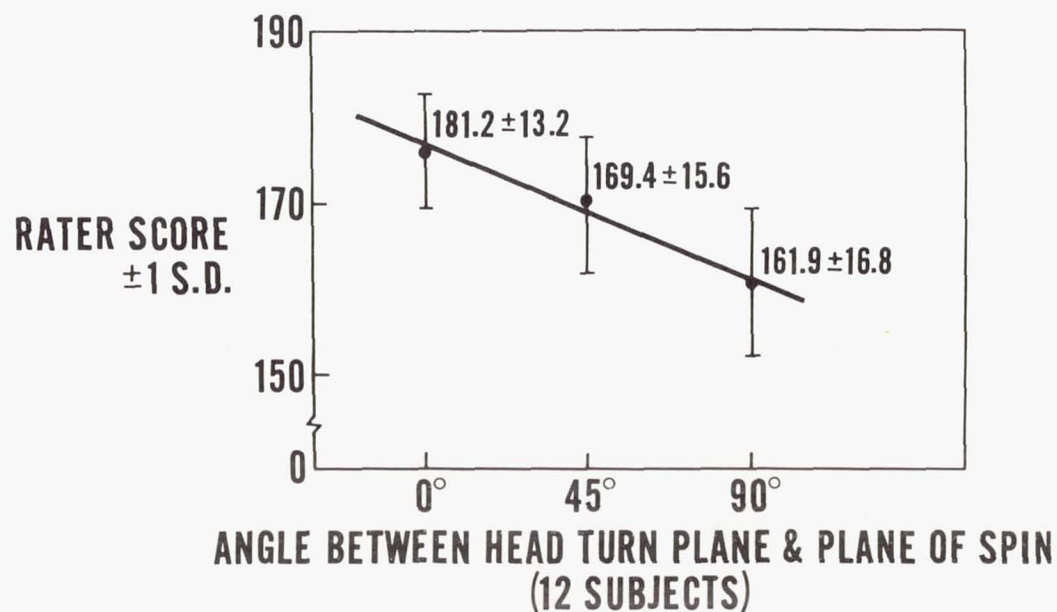
Figure 3.- Monaxial head turn test: performance on rational analysis tester (RATER) vs plane of Z axis head turn.

The purpose of the present study was to extend this technique to permit comparison of the disorientations resulting from head turning (Z axis movements) with those from head nodding (Y axis movements), quantification of these disorientations as a function of the angle separating the plane of head turn from the plane of spin, and exploration of the feasibility of adaptation to head movements in these various orientations.

Such information could then be analyzed to provide guidelines for design envelopes in which displays and controls could be positioned with minimal penalty to the engineering design or the astronaut.

METHOD

As in the preliminary study, the spin rate of 12.2 rpm at the selected test radius provided 1g radially, inclining the floor of the simulator 45° from its static horizontal, with the gravito-centrifugal resultant at right angles to the simulator floor. In this study, however, a chair was constructed to incline the subject 45° on his side (fig. 4) rather than on his back. This position still maintained his Z axis at a constant angle of 45° from the inertial resultant for any chair orientation. At 12.2 rpm, with the subject facing the direction of centrifuge spin, head turns about the Z axis were perpendicular to the spin plane (creating maximum Coriolis effect), while head turns (or nods) about the Y axis were in the plane of spin (creating minimal Coriolis effect). When he faced against the direction of spin the opposite was true: Y axis turns were 90° out of the plane of spin and the Z axis turns were in the plane. Halfway between, when facing the spin axis, both his Z and Y axis head turns were 45° from the plane of spin. (See table I.)

TABLE I.- ORIENTATION ANGLES AS FUNCTIONS OF SUBJECT POSITION

Subject orientation to motion	Position	Between spine and resultant, deg.	Between head turn plane and spin plane, deg.	
			Z axis	Y axis
Forward	1	45°	90°	0°
Backward	3	45°	0°	90°
Toward center of rotation	2	45°	45°	45°
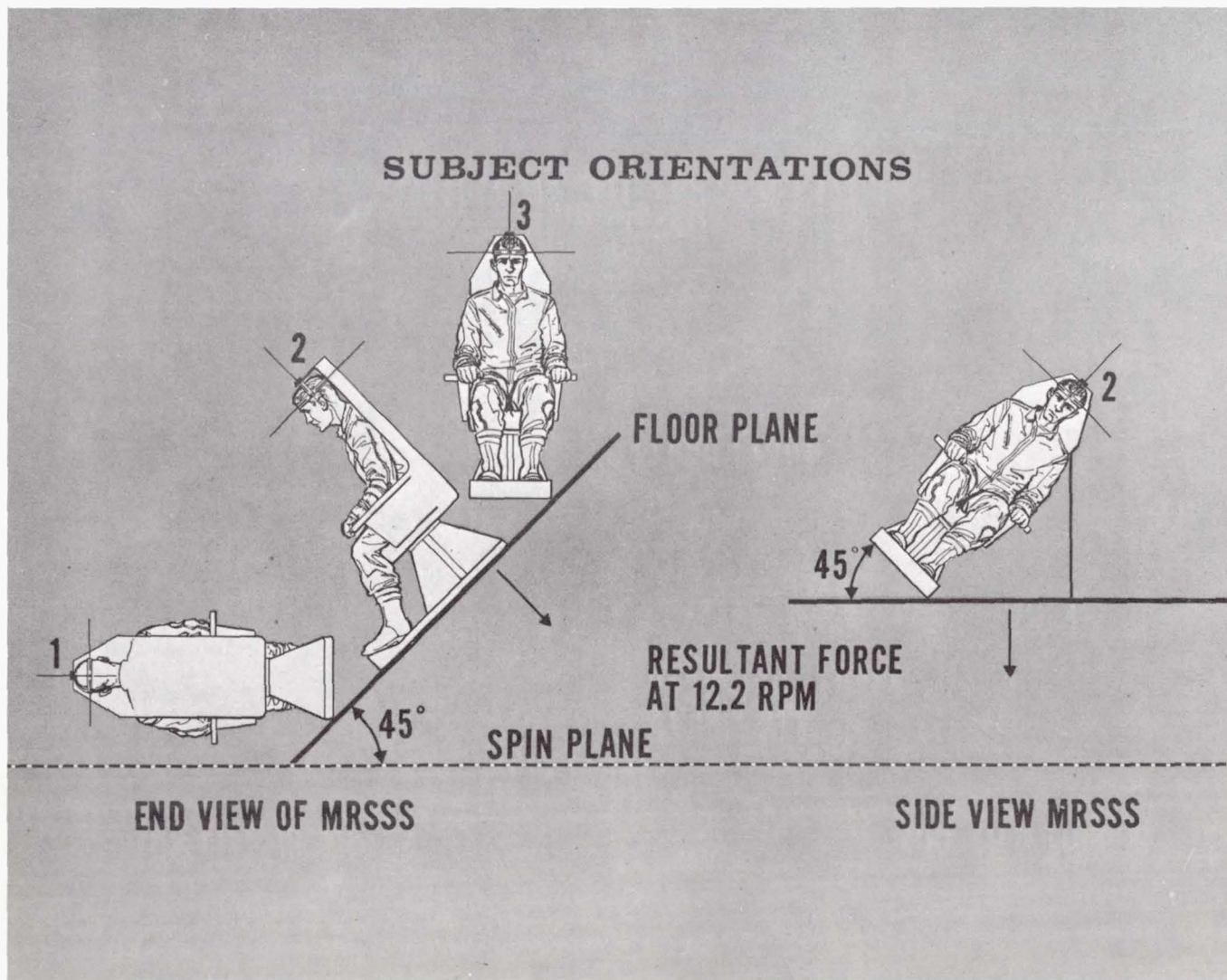
Figure 4.- Biaxial head turn test: relation of plane of Y and Z axis head turns to plane of MRSS spin.

Figure 5 is a picture of the chair and shows the head restraint system. Head motions were restricted to exact planes by use of a double ball-bearing circular race for the Z axis motions, an adjustable sleeve bearing for the Y axis motions, and stops for both degrees of freedom. A number of adjustments were available, and needed, to provide full ease of head movement, especially in Y axis movements. Anthropometric differences greatly affected the point of Y axis rotation and there was also considerable difference in the way the head was nodded. Some subjects used most of the cervical area in the motion, others flexed primarily at the atlanto-occipital joint. It was found that both Y and Z turns had to be completely comfortable for the subject or he fatigued quickly.

Figure 6 shows the adjustment required to accommodate the range of body types represented by the subjects. Both the Y and Z axis turns were recorded by a Grass polygraph from potentiometers mounted at the centers of axis rotation. Readouts were calibrated prior to testing each subject.

The apparatus used to measure performance following each head turn was the Logical Inference Tester (LOGIT). The subject's console contains 20 buttons, each of which lights when pressed. This console is connected to the test administrator's console, the latter permitting programming of the sequence in which the buttons must be pushed in order to illuminate the entire panel. When the buttons are pushed in the correct sequence, the lights stay on, but if an error is made, those lights out of proper sequence go off when a sequentially preceding button is eventually pushed. This informs the subject an error was made and provides clues as to its correction. There are several ways the LOGIT can be utilized, but for this experiment, only one sequence was used. The subject was required to memorize this sequence and to become proficient in its repetition prior to the static baseline test. This usually required about 1 hour.

The subject was then placed in the chair and trained for an additional 30 minutes using the complete test format. A starting light was placed in a position that required the subject to make a 70° head turn about either his Y or his Z axis, on his left for the Z axis, or above his head for Y axis. Between each LOGIT trial the subject was instructed to immediately return his head to the starting-light viewing position.

Each orientation test sequence consisted of ten 15-second trials separated by nine 20-second rest periods. Previous tests in the MRSSS had indicated the importance of allowing adequate time for cupular recovery when attempting to measure disorientation due to head motions. Performance was graded on the total number of buttons pressed in proper sequence during the 150 seconds testing at each orientation.
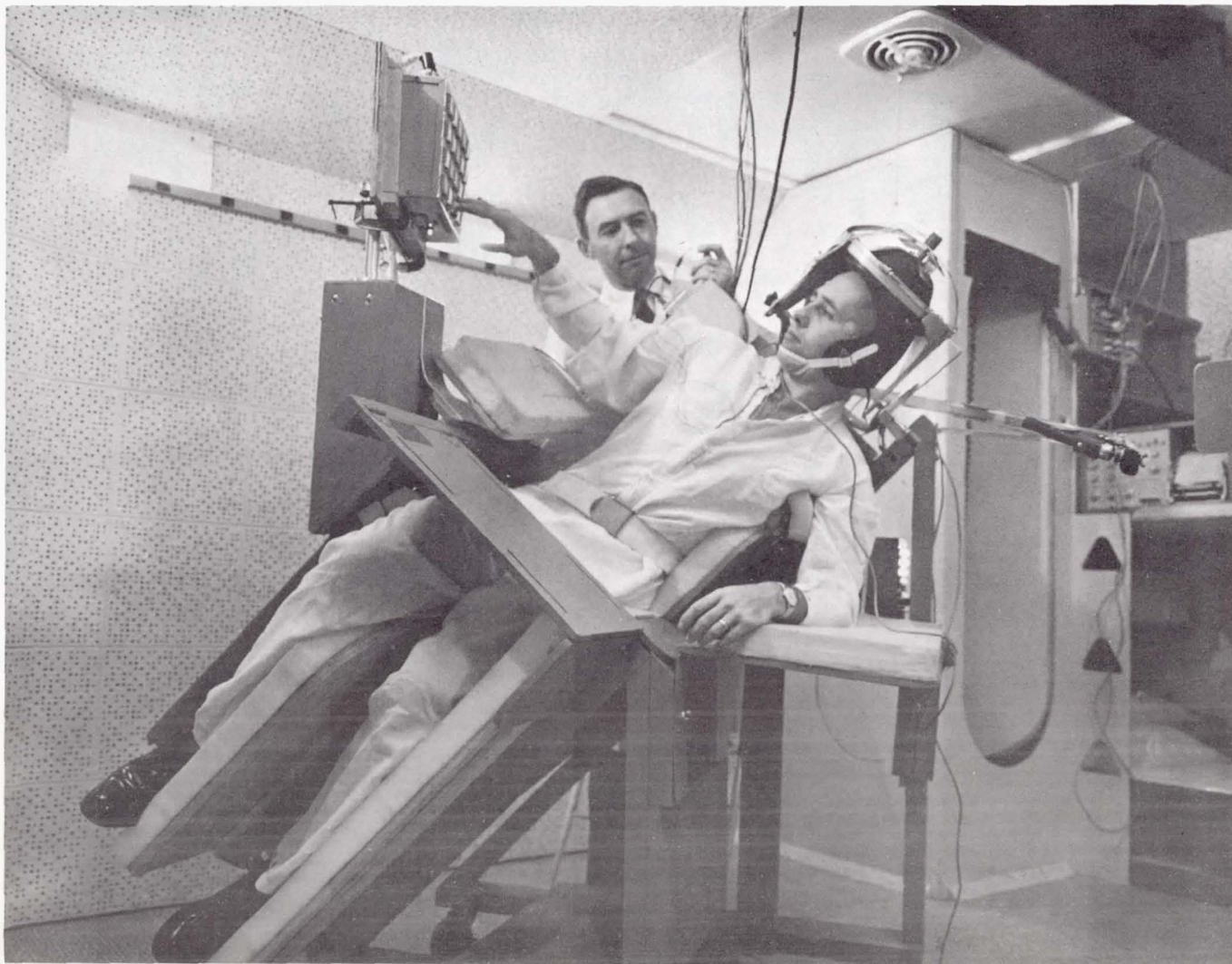
Figure 5. - Biaxial head turn test: subject performing Z axis logical inference test (LOGIT) while seated in head turn chair.
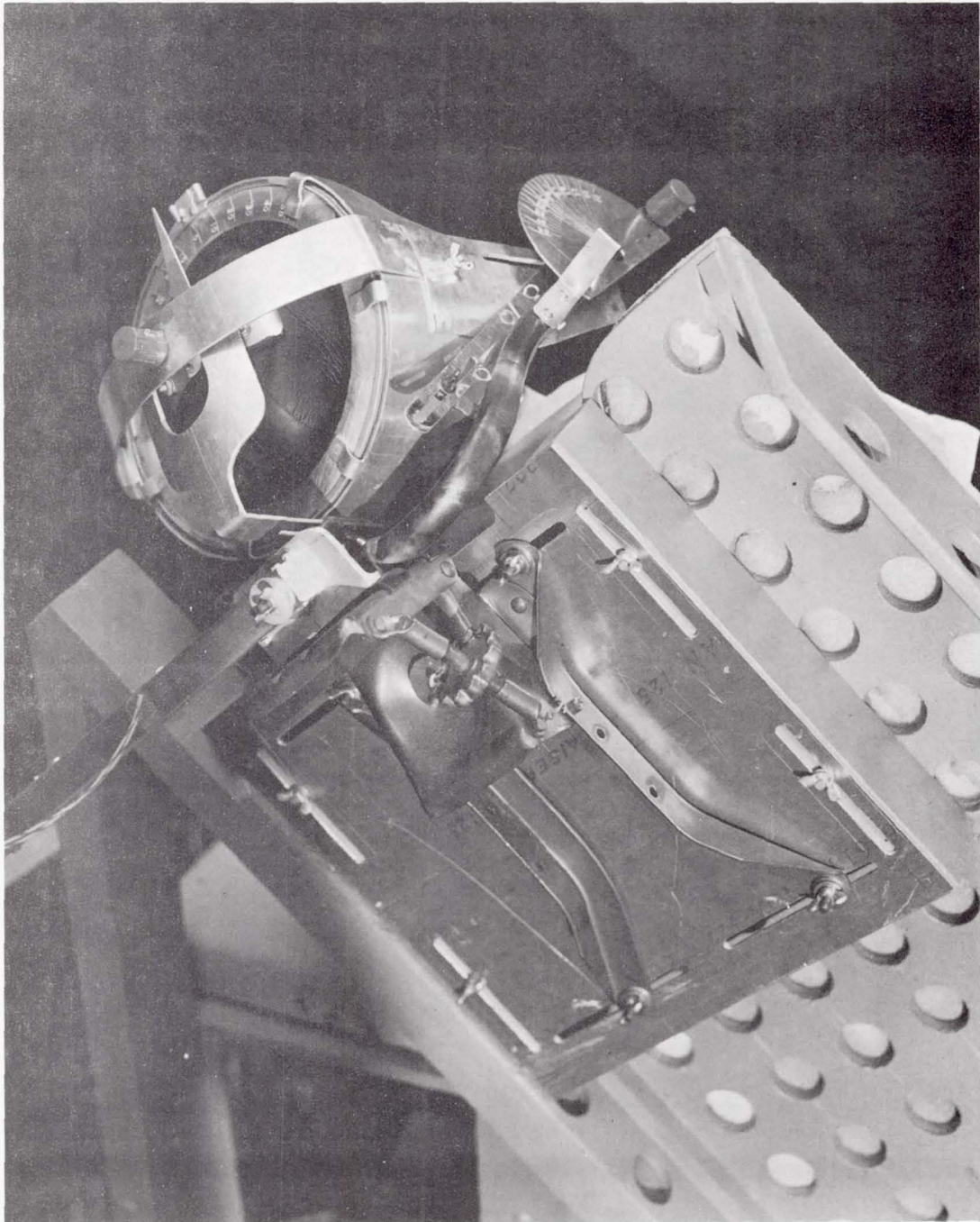
Figure 6. - Biaxial head turn test: rear view of adjustable head restraint.

There were six orientations (0°, 45°, and 90° for Z and Y head turns). After the first three sequences (either Z or Y) were completed, the simulator was stopped and necessary adjustments made to convert the head turning restraint to the other axis. Each axis sequence took about 45 minutes so the subjects were at 12.2 rpm for a total of 1 hour and 30 minutes.

Each orientation could be expected to have an effect on the tolerance to the succeeding head turn sequences. To null this effect, each subject performed a different permutation of orientations. The subject number was dictated by the number of major permutations of two axes movements and three head-turn angles to the plane of spin. Twenty-four subjects were required to complete all the test permutations, each permutation being represented by one subject. Two subjects were tested each day, 3 days a week.

Navy jet pilots were used as subjects to provide a sample that was reasonably homogeneous and qualitatively similar to spacecraft personnel. To simplify chair construction, only right-handed subjects were used. The subjects varied between 25 and 40 years of age and were all active aviators. The motivation and cooperation of the group was exceptional in all cases. Subjects were instructed to avoid turning their heads to the point of overt motion sickness. Whenever they felt that one more head turn might initiate vomiting, they skipped that trial and took a zero score. Using this approach, 24 subjects were able to complete all six orientations, and all but 5 subjects completed all trials. The onboard test conductor and offboard test monitor exchanged positions to limit personal exposure to 45 minutes duration or 1 hour and 30 minutes per day at the 1.4g resultant. This was done as a precaution because of the small amount of information available on tolerance to repeated exposures to plus g in the Z axis.

RESULTS

All but one subject felt the Y axis movements were easier than the Z axis movements in all orientations. The one subject who felt there was no stress difference between the Y and Z axes showed higher scores for the Y axis orientations than for the Z. All subjects were able to correctly rate the disorientation for the increasing angle between plane of head turn and spin plane for both Y and Z axes.

Figure 7 shows the number of buttons pushed in correct sequence for an average 15-second test trial for all Y and Z axes head motions during static and perrotatory testing. The scores are overall means

MEAN PERFORMANCE AS NUMBER OF CORRECT RESPONSES VS INTER-AXIAL ANGLE
FOR ALL TEST ORIENTATIONS
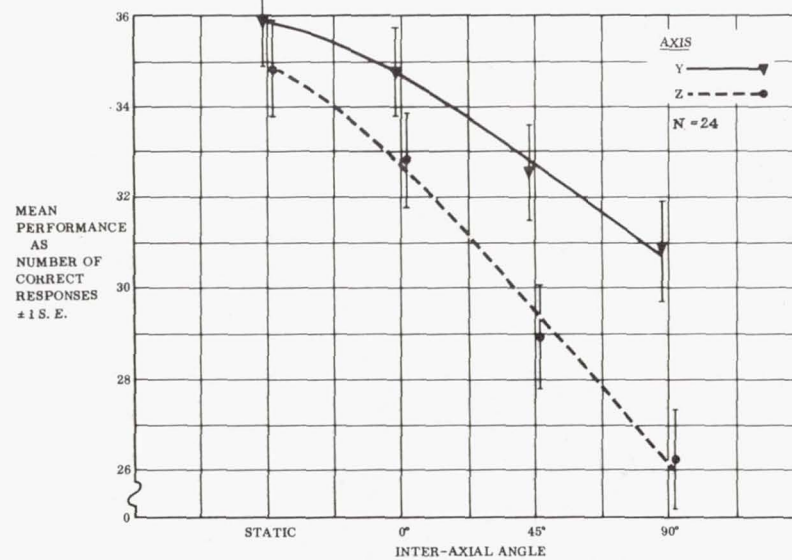
Figure 7. - Biaxial head turn test: LOGIT performance vs plane of head turn.

for 24 subjects and the standard error (S.E.) of each mean is shown. The subjective feelings are substantiated by the consistently higher scores obtained in all orientations for the Y axis.

The mean overall head turn time for all subjects in each orientation is shown in figure 8. The head turn time was calculated from the poly-graph traces and this is the time required to turn the head 70°. Again the Z axis appears to be much more of a stress. For 90° out of the spin plane, the Z axis time is dramatically increased to almost twice its static value, while the Y axis motion shows a lesser increase.

Figure 9 demonstrates the rapidity with which adjustment to the stresses of certain head turns occurs. Each 150 seconds of testing in each of the six orientations was divided into 10 separate trials. When these trial performances are plotted it is seen that the Y axis move-ment at the 45° orientation appears to be close to the limit for habitu-ation for this length of time. Little, if any, significant improvement occurs during the Y axis 90° test and Z axis head turns show progressive degradation in both 45° and 90° positions. Inability to make a head turn or to start the trial was scored as a zero and this occurred more frequently with the Z axis turns than with the Y sequences.

Table II shows the significance of the differences observed in performance and head turn time as a function of the head orientation to the spin plane; $P \leq 0.05$ was considered significant.

DISCUSSION

The test results provide quantitative substantiation of the theo-retical conclusions and subjective findings of earlier investigators that head turns in a revolving space station should preferably be executed in the plane of the system rotation for optimal performance during crew adaptation to rotation. Coriolis effects on the labyrin-thine organs have long been of concern to the Graybiel group at Pensacola and more recently have been under intensive study in our laboratory. A recent study in the Revolving Space Station Simulator for 5 days at 6 rpm demonstrated the extreme adaptability of motivated humans to a rotational environment. All four subjects completely adjusted to the rotation in less than 48 hours. One subject, who had previous exposures to rotation, could make any motion in any plane without disorientation or any other sensory disturbance after 12 hours. His adaptation was dramatically rapid and complete in spite of normally sensitive labyrinths. The authors believe the trunnioned room had much to do with this adapta-tion, as it allowed the subjects a conventional visual and inertial reference, with the apparent vertical always perpendicular to the floor.

MEAN HEAD-TURN TIME VS INTER-AXIAL ANGLE
FOR ALL TEST ORIENTATIONS
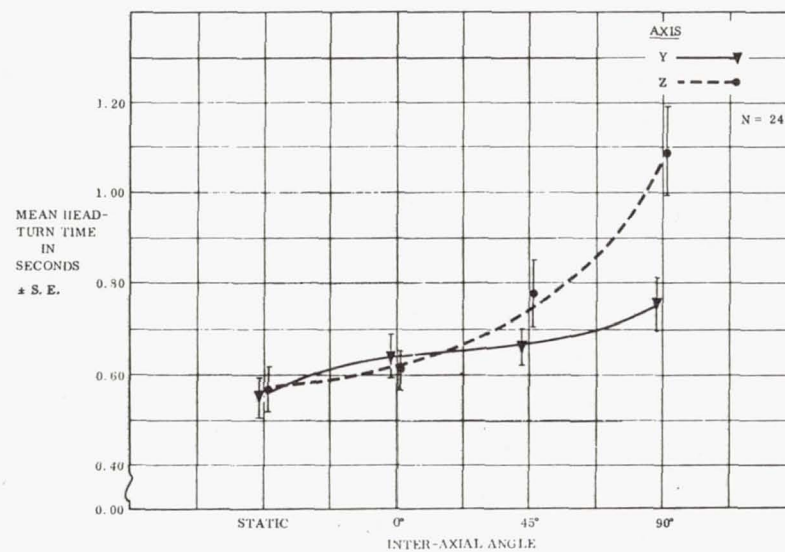
Figure 8. - Biaxial head turn test: head turn time vs plane of head turn.

MEAN PERFORMANCE AS NUMBER OF CORRECT RESPONSES VS. TRIAL NUMBER
FOR ALL Ss: FOR ALL TEST SEQUENCES
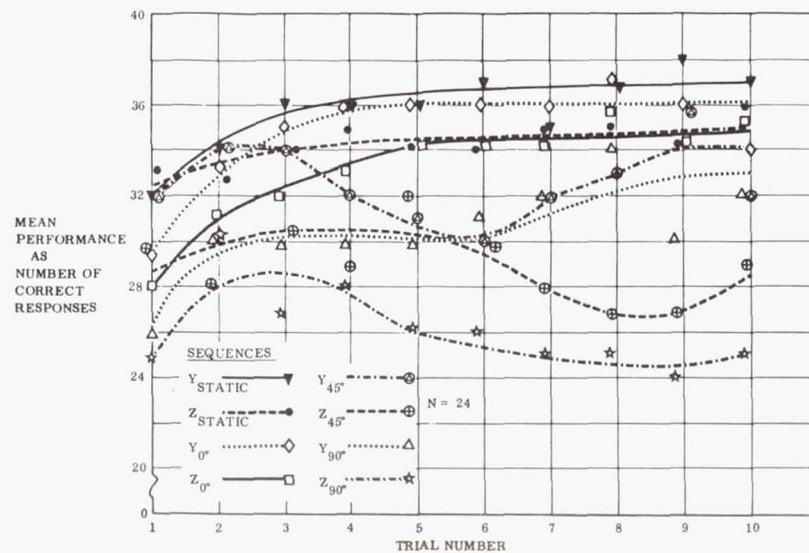
Figure 9. - Biaxial head turn test: LOGIT performance vs test trial number
for all head orientations.

TABLE II.- RESULTS: ANALYSIS OF VARIANCE

24 subjects, orientation vs performance efficiency			

Within Y turns   Within Z turns

$Y_{45} < Y_S,$*   P < 0.01 $Z_{45} < Z_S$ and $Z_0,$ P < 0.01

$Y_{90} < Y_S$ and $Y_0,$ P < 0.01 $Z_{90} < Z_S$ and $Z_0,$ P < 0.01

$Y_{90} < Y_{45},$ P < 0.05 $Z_{90} < Z_{45},$ P < 0.05

Between Y and Z turns

$Z_0 < Y_S,$ P < 0.05 $Y_{90} < Z_S,$ P < 0.01

$Z_{45} < Y_S$ through $Y_{45},$ P < 0.01 $Y_{90} < Z_0,$ P < 0.05

$Z_{90} < Y_S$ through $Y_{90},$ P < 0.01

24 subjects, orientation vs head turn time

$Z_{90} >$ all others,   P < 0.01

*S = static.

This·is the major reason it is considered important to provide a
constant Z axis displacement from the vertical in all of the orientations
used in the experiment reported here, for such adaptation can thus be
anticipated in the artificial g system. From the results of these
laboratory studies, it appears that man is capable of supressing (or
compensating for) disorienting signals from the labyrinth, particularly
if they are not required for his adjustment to the environment. This
is not surprising as there are many other examples of this, such as
exclusion of one eye in severe diplopia, or simple auditory adjustment
to a constant background noise.

Though these findings should find use in spacecraft design, the
constraints they may impose will probably be temporary in nature and
will apply mostly to the equipment necessary for operations during the
adaptation period. Means for accelerating this adaptation such as pre-
launch exposures to rotation are certainly feasible.

It is of interest that the regression curves for the Z axis tests
in both the preliminary and the more comprehensive approach have the
same slope. The two experiments used different performance tests and
in one case the subject was inclined on his side, the other on his
back. The first experiment was done on aviators of propeller aircraft
and the latter on jet pilots. This suggests a somewhat constant ratio
of performance degradation as head turns move out of the plane of spin
in the Z axis.

CONCLUSIONS DRAWN FROM RESULTS

Head motions out of the plane of spin become quantitatively more
disorienting as the angle approaches 90°.

Y axis head turns are significantly easier than Z axis head turns
in an environment rotating at a highly stressful rate.

Adaptation to such a rate appears to take place rapidly for those
head turns performed near the plane of spin, but becomes increasingly
more difficult as the interplanar angle increases. Though 45° out of
the plane of spin appears to be tolerable for Y axis head movements at
this spin rate, it appears to be unacceptable for Z axis head movements.

SIGNIFICANCE FOR MANNED SPACEFLIGHT

If rotation is used to provide an inertial force within a space-craft, proper orientation of displays and controls should be provided, especially during the period of habituation to the rotation.

In space, the spinal (Z) axis of the crewman will be in the plane of spin much of the time (aligned with the centrifugal vector). The Z axis head movements will then be in a plane 90° out of the spin plane - the movements shown to be most disorienting. The displays and controls to be used during the first few days of rotation should, therefore, be arrayed in the apparent vertical dimension so that Y axis or nodding motions can be favored in monitoring.

The envelope for monitoring requirements can probably be plus or minus 45° from center (spin plane) on either the leading or trailing bulkhead when vertically arranged displays are used.

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A RESUME OF THE EFFECTS ON THE CHIMPANZEE OF RAPID DECOMPRESSION

TO A NEAR VACUUM

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It was the goal of this research program to determine the behavioral, physiological, and pathological sequelae of rapid decompression of chimpanzees to the near vacuum, in order that mission rules and safety procedures might be incorporated into manned spacecraft.

Up to this date 16 decompressions to less than 2-mm Hg involving 15 chimpanzee subjects from the 6571st ARL, have been successfully made at the Aeromedical Research Laboratory, Holloman Air Force Base, New Mexico.

The problem was solved in two separate sequences. The first series established data points for exposure times to the vacuum of 5, 30, 60, 90, 120, and 150 seconds (in all, nine decompression tests). The second series, which is still in progress, endeavoured to establish greater reliability of the results obtained from exposure values of 90, 120, and 150 seconds by replicating these exposures.

PERFORMANCE

All decompression subjects underwent intensive training on a complex behavioral program, which was composed of the following schedules:

1. Continuous motor task (12 min).- To avoid an electric shock the subject was required to depress a lever at least once every 5 seconds. Performance was measured by response rate per minute and an efficiency measure of avoidance of the electric shock.

2. Discrete avoidance reaction time tasks.- Superimposed upon the continuous avoidance task were reaction time tasks to three different visual cues and one auditory cue, which had to be attended to within 1 second to avoid electric shock. A total of 51 such discrete events

occurred during the 12 minutes of continuous avoidance. At times, these stimuli were presented in pairs and still had to be extinguished within 1 second. The behavioral measures taken were reaction times and efficiencies on all parameters.

3. Oddity discrimination tasks (10 minutes).- In the second portion of the behavioral program, the subject was required to discriminate an "odd" symbol of three geometric symbols presented; two figures were alike and one figure (the correct one) was different or "odd". Eighteen such problems were dispersed over the 10-minute period. The procedure was corrective, i.e., an incorrect choice repeated the same problem until a correct choice was made. By selecting the "odd" symbol the subject was rewarded by avoiding an electric shock as well as receiving a choice of food or water. The measures taken were discrimination, efficiency, and reaction time.

The subjects were restrained in a formfitted couch with the performance panel in an overhead position. All subjects were monitored for electrocardiogram, respiration, heart rate, and skin temperature, while 10 subjects were fitted with cortical electroencephalogram electrodes. Figure 1 shows the performance panel.

During the first series of nine decompression tests, each subject was transported to the decompression chamber 2 days prior to the experiment. To obtain baseline data on the behavioral as well as physiological parameters the subject was installed in the chamber and maintained at ground level atmospheric pressure for 8 hours.

On the day of the experiment the subject was placed in the chamber and the chamber door was sealed and the subject was provided with a 100-percent-oxygen environment for the purpose of 3 hours of denitrogenation before going to altitude. Temperature and humidity were maintained at 24° C and approximately 35 percent, respectively.

After 3 hours, the subject was subjected to a pressure altitude of 179-mm Hg (35 000 ft) and held at this pressure altitude for 35 minutes. At this time, decompression of the experimental chamber occurred within 0.8 seconds to a pressure of less than 2 mm of mercury (150 000 ft). The subject was held at this pressure altitude from 5 to 150 seconds, depending on the experiment. Recompression to 179 mm mercury was done within 30 seconds with 100-percent oxygen. This environment was maintained for 24 hours after decompression, then, the subject was removed and taken to the Veterinary Division for medical examinations.

As long as the subject remained in the experimental chamber, performance programs were presented at fixed intervals. The actual decompression was locked on to the onset of the third minute of a performance
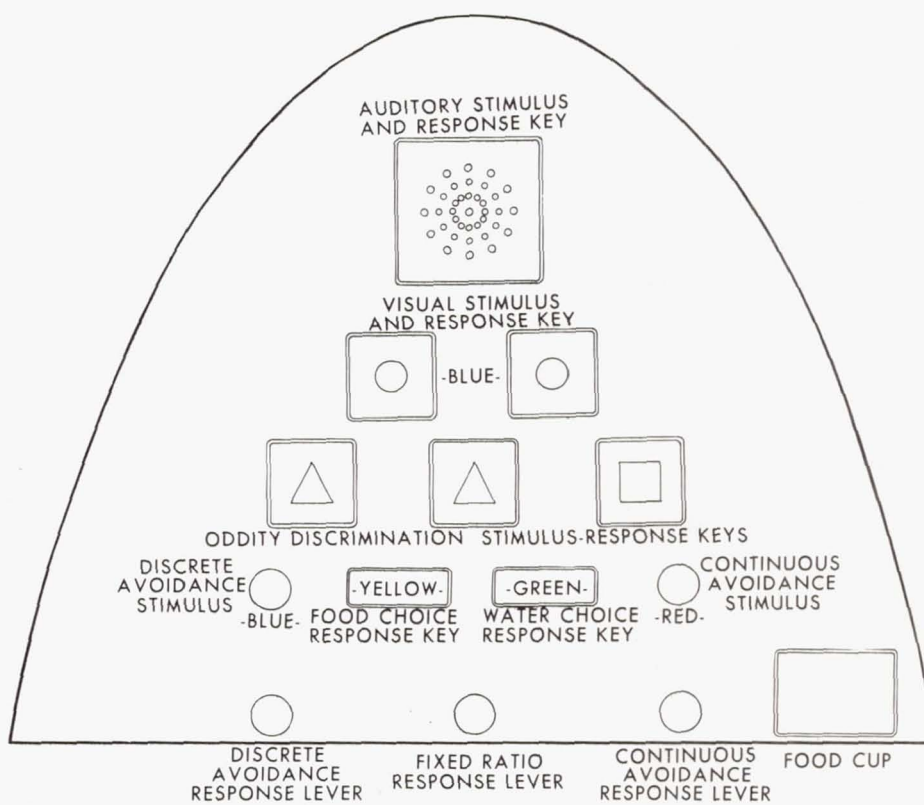
Figure 1. - Schematic drawing of the performance panel.

schedule to determine the time of useful consciousness (the last response to a meaningful stimulus) and the time of total behavioral impairment (the first response after the animal regained consciousness). A third temporal measure was determined by establishing the point in time after decompression-recompression when the subject was again performing on all behavioral variables within its baseline range of performance. This measure we called total behavioral recovery.

Based on the findings of the first series, the second (replication) series were changed as follows: the time in the chamber post decompression was reduced to 4 hours and the baseline data was collected in an environment more similar to the actual experiment, i.e., the subject was provided with the identical physical environment as on the test date (100 percent oxygen, 3 hours of denitrogenation, ascent to 179-mm Hg, and 4 hours post decompression confinement in the chamber), except that the actual decompression was omitted. Figures 2, 3, 4, 5, and 6 are photographs of the test equipment and subject.

RESULTS

A summary of the behavioral results is presented in figure 7.

Figures 8, 9, and 10 show data collected from the first nine decompression tests (small circles). Based upon these points, predictions were made as to the expected performance values at certain exposure times. Data points from the second sequence of decompression were inserted into the graphs (larger, crosshaired circles) to demonstrate that the experimental controls were sufficient to allow verifyable predictions as to the expected values for total time of impairment and total behavioral recovery between 5 and 150 seconds of exposure to the vacuum.

Statistical comparisons between baseline and experimental performance for some animals showed some significant improvement on the complex discrimination task, which is of considerable importance because it suggests negligible trauma to the central nervous system.

Other subjects showed a number of decrements, primarily, in the reaction time parameters to discrete stimuli. It should be noted, however, that these differences often lay in the hundredths-of-second range and would generally not be of operational significance.

The fact that statistically significant decrements in performance did occur during the experimental period, and the fact that all subjects did return to a baseline level of performance while still in the
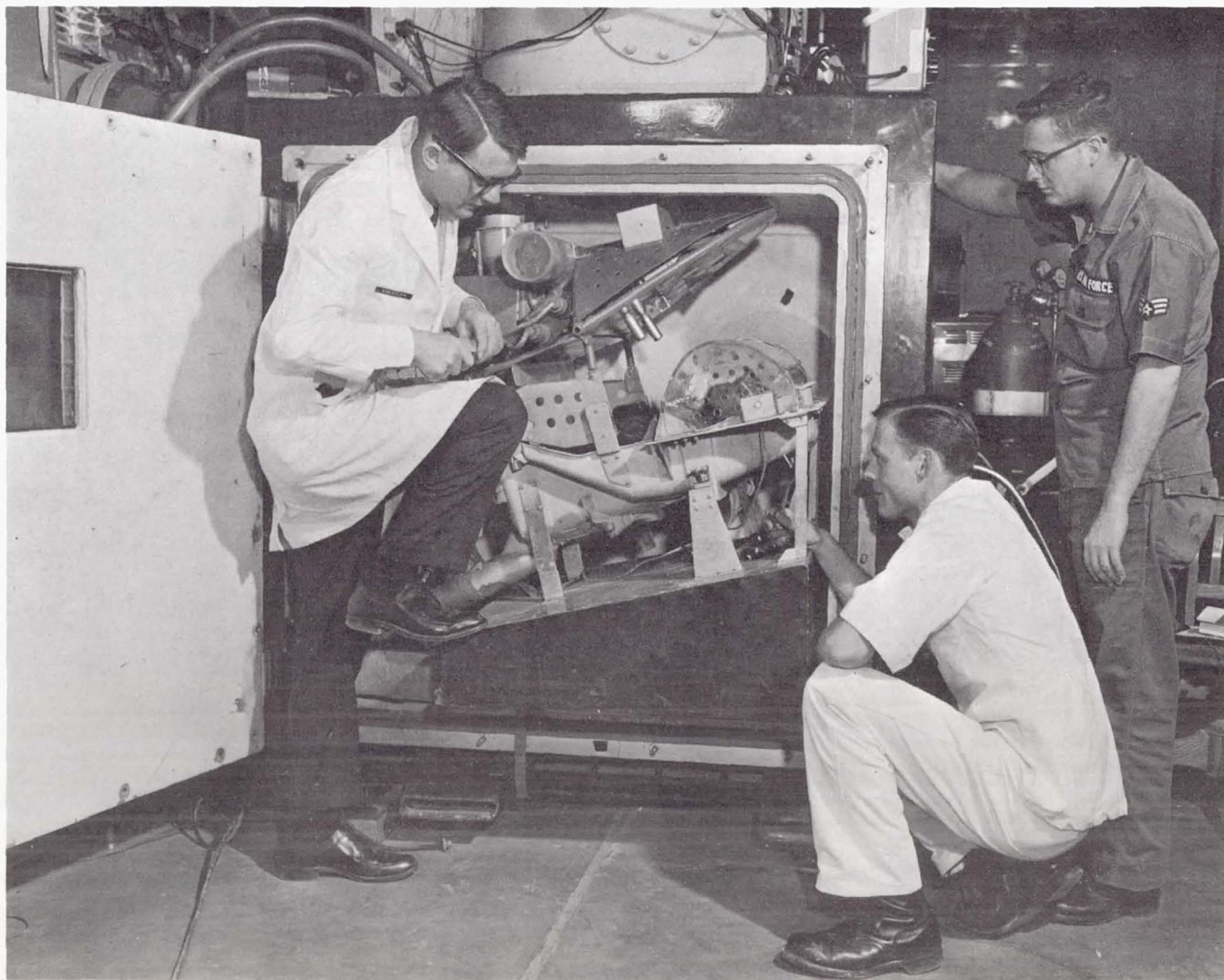
Figure 2. - Biomedical and programming leads are connected.
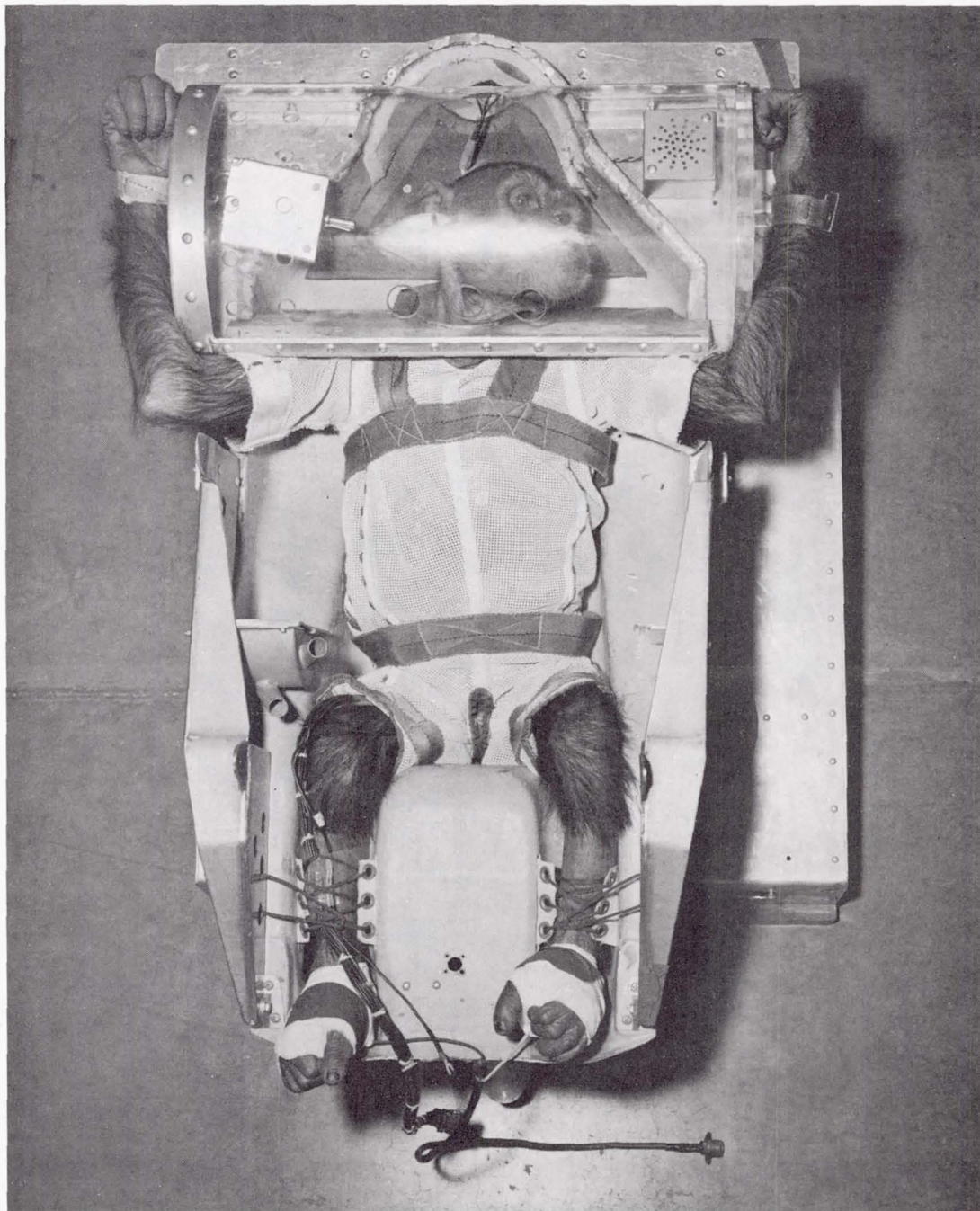
Figure 3. - Subject is fully instrumented and restrained in a couch.

64-A268 E 29 June 64 Land-Air
Rapid Decompression Tests Uncl.
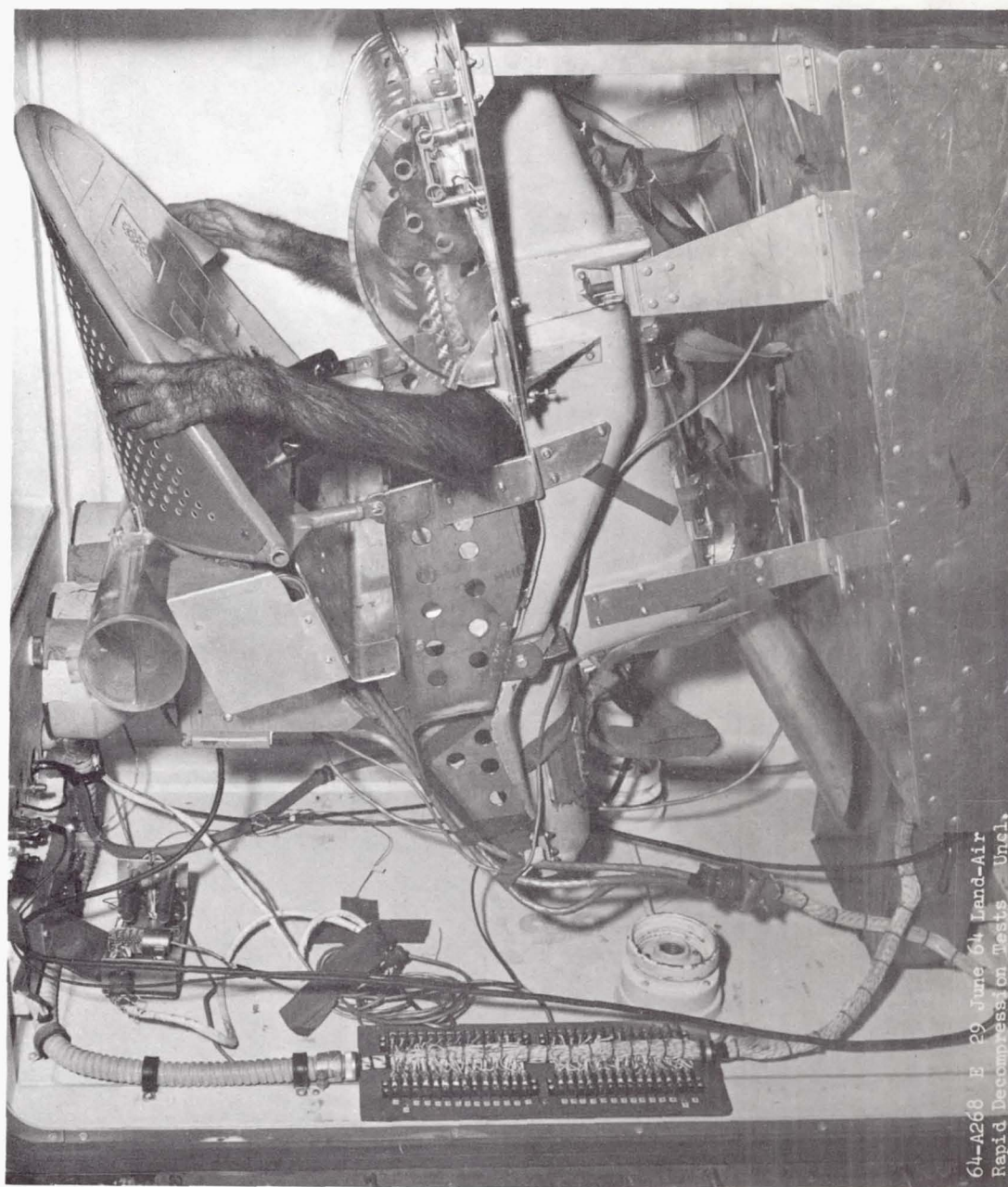
Figure 4. - Subject inserted in decompression chamber.
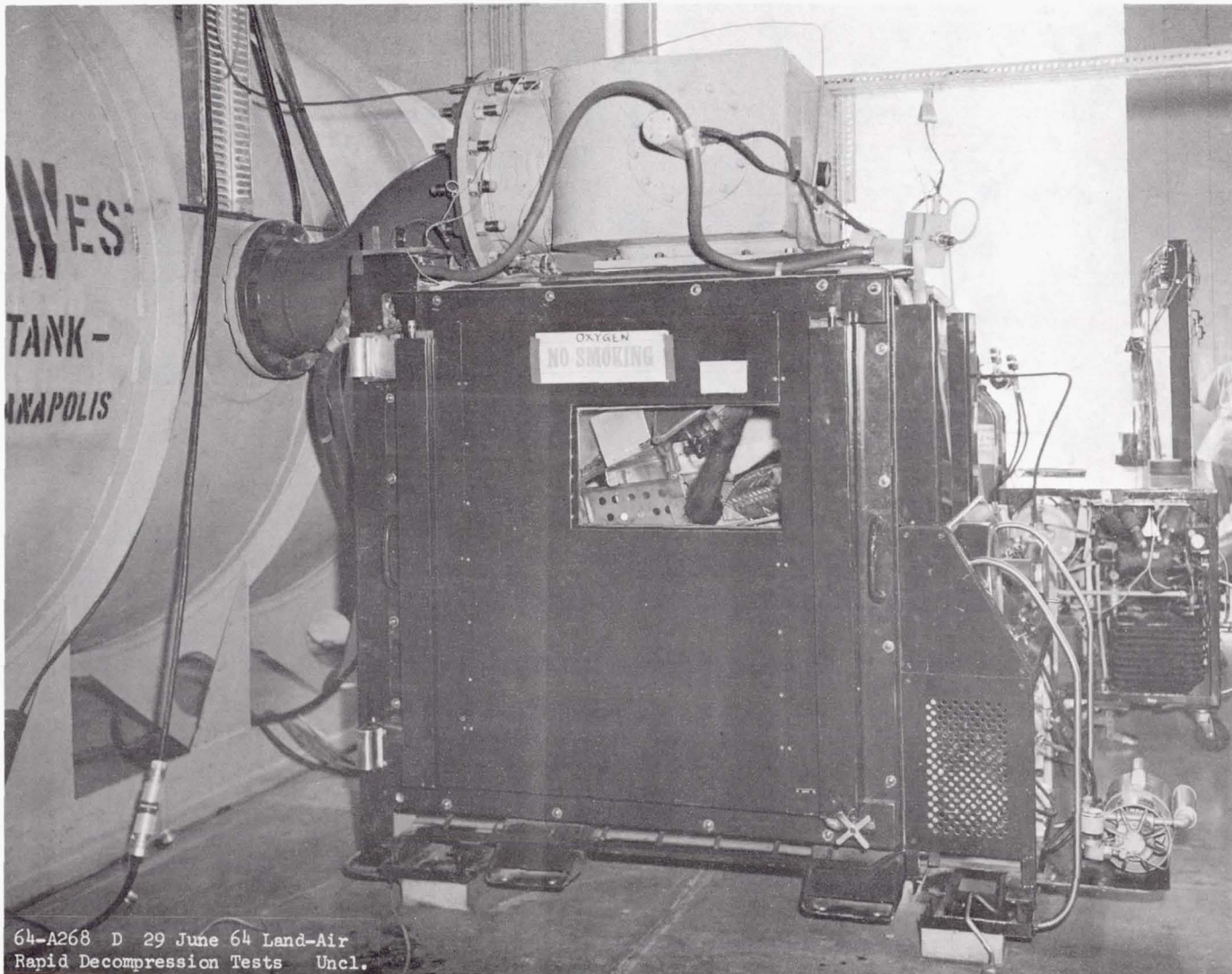
Figure 5. – Decompression chamber with subject inside.

64-A268 D 29 June 64 Land-Air
Rapid Decompression Tests   Uncl.
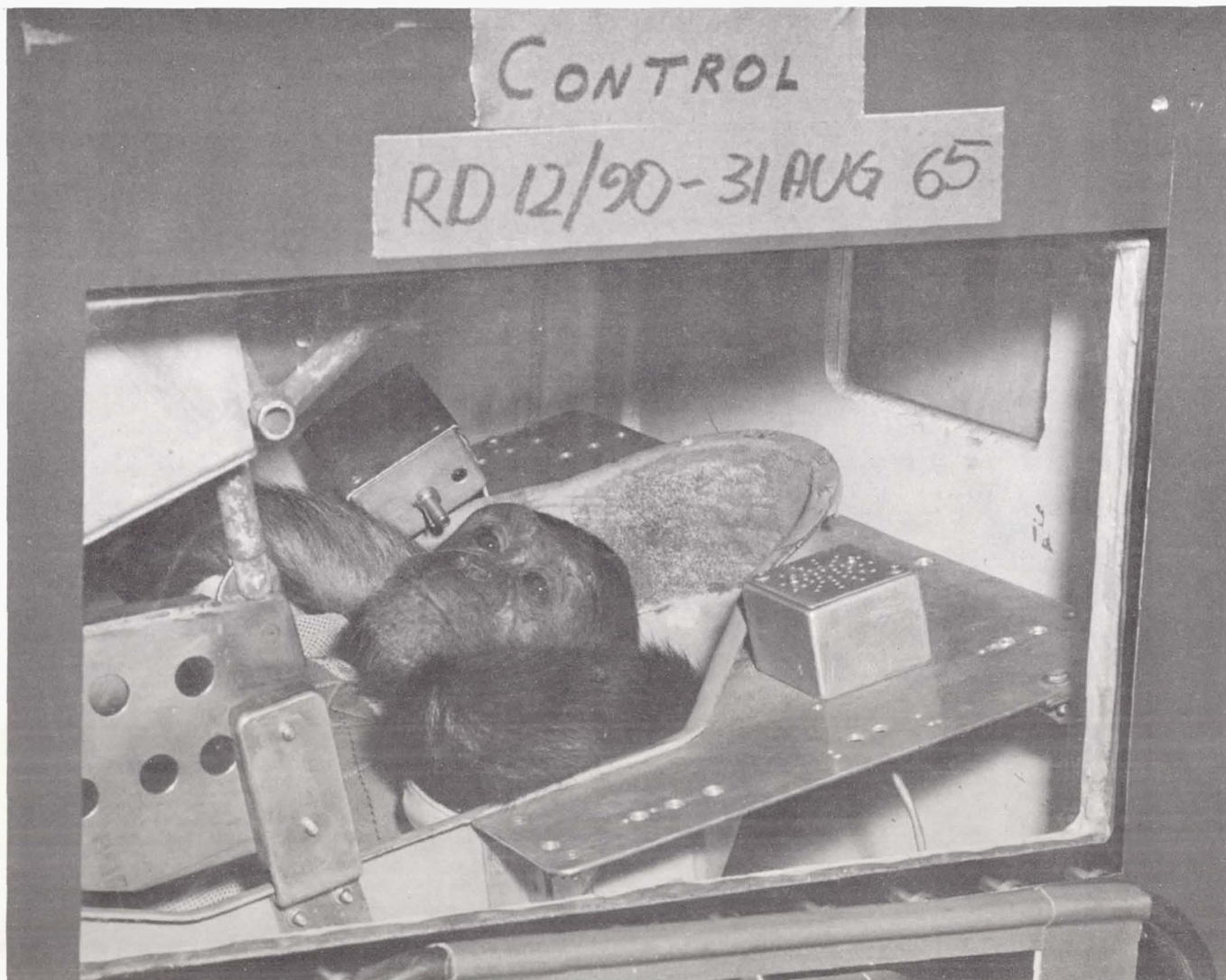
Figure 6. - Resting subject.

Summary of Rapid Decompression Effects

RD Experiment	Exposure Time to < 2 mm Hg (seconds)	TUC Time of Useful Consciousness (seconds)	TTI Time of Total Behavioral Impairment (minutes)	TBR Time of Total Behavioral Recovery (minutes)
1	5	11	.42	20.00
2	30	Not Available	1.80	67.00
3	60	16.9	2.48	90.08
4	90	11.3	18.93	163.02
7	90	12.5	4.82	43.00
12	90	3.6	Not Available	Not Available
13	90	6.5	11.63	199.00
16	90	8.0	15.67	188.75
5	120	10.1	8.56	245.02
8	120	9.5	19.07	121.75
10	120	29.6	13.73	81.75
15	120	10.4	12.97	198.5
6	150	29.7	36.56	144.02
9	150	8.0	38.69	247.00
11	150	10.0	46.50	187.00
14	150	1.5	34.83	197.25

Figure 7. - Summary of decompression effects.
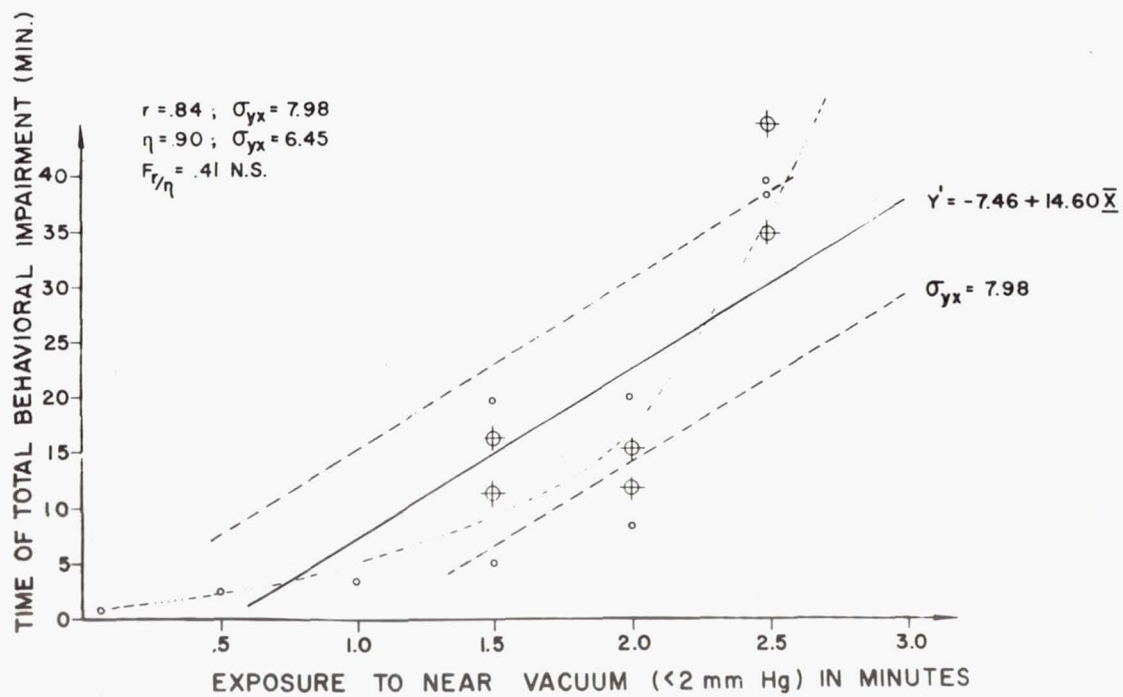
Figure 8. - Relationship between exposure time to near vacuum and time of total behavioral impairment.
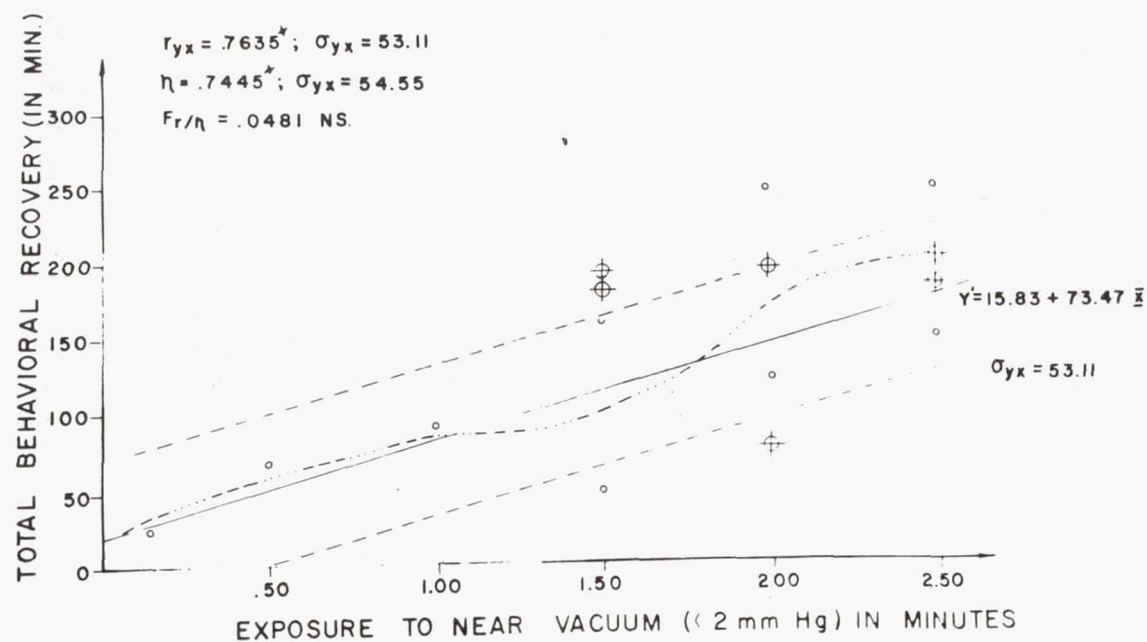
Figure 9. - Relationship between exposure time to near vacuum and total behavioral recovery.
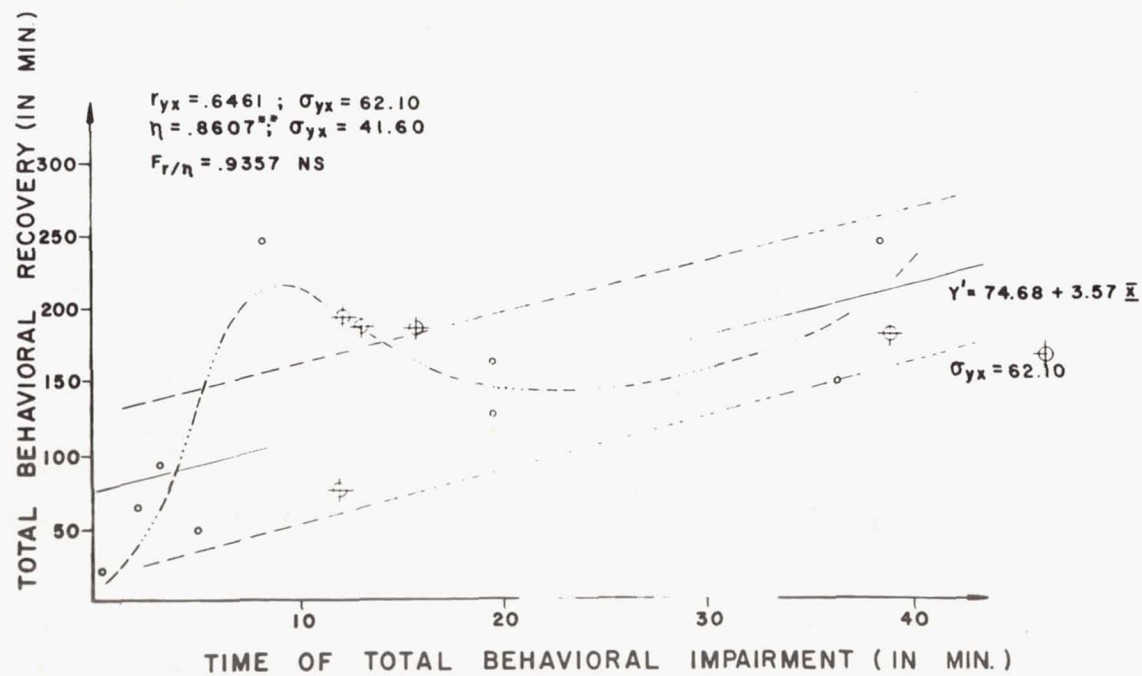
Figure 10. - Relationship between time of total impairment and time of total behavioral recovery.

experimental situation is only a seeming contradiction. The experimental data included all responses following rapid decompression; data did reflect a distinct decrement in subject reaction time, efficiency, and rate of response during the period immediately following recovery. Although each subject returned to a baseline level of performance while still in the chamber, these initial decrements were sufficient to lower the overall experimental means and bring about a statistical difference. Three, six, nine and twelve months post decompression follow-up testing substantiated this point by failing to produce evidence of gross changes in the behavioral performance of the subjects.

Electroencephalogram activity was recorded in the following manner: Decompression subjects one, two, three, four, five, and six had nylon and stainless steel electrodes mounted through the skull in three bilateral locations (frontal, central, and occipital) in contact with the dura. Decompression subjects eight, nine, and ten had stainless steel screws placed bilaterally in the skull at four locations (frontal, central, parietal, and occipital). The leads were brought together under the scalp to an electrical recepticle.

Electrocardiogram electrodes were of the suture type. Electrodes for lead A were located on mid-sternum and over the 5th lumbar vertebra with the ground lead located over the 8th thoracic vertebra. Electrodes for lead B were located on the lower right axilla and on the left inner thigh.

Figures 11, 12, and 13 are a typical physiological record and reads as follows (actual case, decompression test number 6 with 150 seconds of exposure to the near vacuum)!

At T + 37 seconds EEG enters into electrical silence following the end of useful consciousness. One minute later the heart slows from a normal 90 to 60 beats per minute. At recompression (T + 2 min 30 sec), the heart rate is increasing until it reaches 180 beats per minute and respiration begins. The electrical silence in the cortex does not change for another 70 seconds at which time high amplitude slow waves occur.

This type of activity continues and increases slightly in frequency. Twenty minutes following rapid decompression the first signs of a faster rhythm can be noted. For the next 10 minutes, after a series of electrical shocks, received during the behavioral program, these faster rhythms become more noticeable. Six minutes later, at approximately T + 36 minutes, although there is still a large amount of slow activity, the faster activity of 10 to 12 cps is clearly and continuously superimposed. At T + 77 minutes, the record is similar yet somewhat slower to the pre-experimental EEG record.

9 SEPT. 1964

SUBJECT RD 6/150" SHIRLEY (116) FEM.

WEIGHT: 18.64 KG   AGE: 61 MO.

DECOMPRESSION TIME: 150"

TUC 29.7"   TTI 37'3.3"

CARB 72'   ARB 142'0"

RF—RC

LF—LC

LC—LO

LEAD B ECG

LEAD A ECG

RESP

FIG 9-A T-2'25"   PRE-RD RECORD   HR 90   RESP 36

FIG 9-B T+37" DECAY OF EEG ACTIVITY   ECG IN BRADYCARDIA
BETWEEN PERIODS OF TACHYCARDIA HR 60   RESP (X)

FIG 9-C T+1'15" ELECTRICAL SILENCE   STILL SOME
RESPIRATORY MOVEMENTS   HR 60   RESP 18

FIG 9-D T+2'25" ELECTRICAL SILENCE   RECOMPRESSION
BEGINS HR 114 RESP (X)

FIG 9-E T+3' ELECTRICAL SILENCE   RESPIRATORY ACTIVITY
BEGINS 10" AFTER THIS RECORD HR 180 RESP (X)

Figure 11. - Physiological records of a 150-second exposure to near vacuum.

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9 SEPT. 1964
SUBJECT RD 6/150" SHIRLEY (116) FEM.
EEG CAL.   • 100 μ V
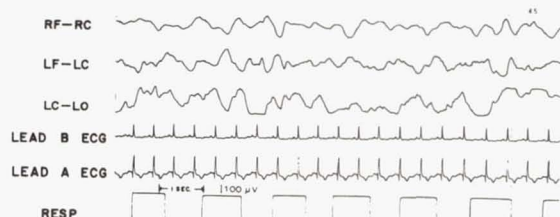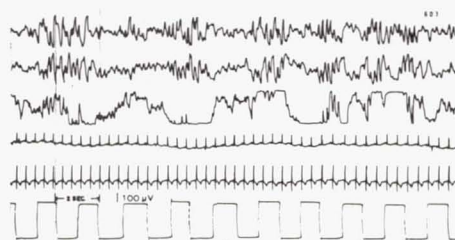
RF—RC
LF—LC
LC—LO
LEAD B ECG
LEAD A ECG
RESP

FIG IO—A T+3'45" BEGIN OF FIRST CORTICAL SLOW ACTIVITY
HR 96 RESP 24

FIG IO—B T+5'25" RETURN OF CORTICAL RHYTHMS WITH
EYE MOVEMENT ARTIFACTS   HR 132 RESP 30

FIG IO—C T+6'20" PROGRESSION TO HIGH AMPLITUDE SLOW
WAVES   HR 126 RESP 36

FIG IO—D T+9'20" INCREASED RHYTHMS   HR 150   RESP 48
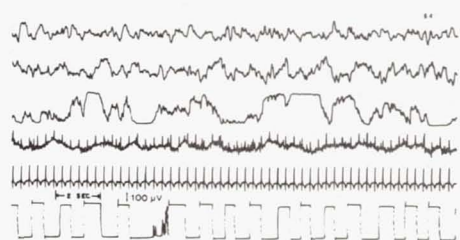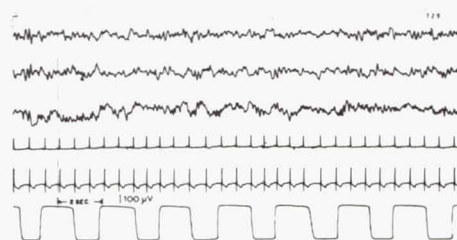
Figure 12. - Physiological records of a 150-second exposure to near vacuum.
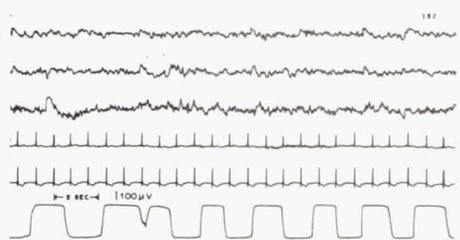
Figure 13. - Physiological records of a 150-second exposure to near vacuum.

There was no readily visible relationship of either heart rate or respiration to performance ability or cortical electrical activity. There was an initial tachycardia at the onset of decompression followed by respiratory arrest and a bradycardia. In the longer decompressions, there was a tachycardia following the bradycardia before recompression and continued after recompression to rates of 198 beats per minute.

Of great importance is the obvious feasibility of using the EEG as an indicator of performance impairment. According to our findings, it would seem that performance will be lowered when the EEG activity is slower than normal. This is not to say that normal EEG dictates normal performance but rather, that without it, fully effective performance does not return.

The use of deep implanted electrodes for the next experiments may show differentiation in brain activity not readily visible in the cortical record. Such procedure is expected to lead to the recognition of subtle patterns related to visual, auditory defects, and perhaps motivational as well as emotional changes.

All subjects, upon initial examination, following the decompression showed slight elevations in neutrophiles and transaminase levels in the blood which are considered normal reactions to stresses of this magnitude. Several of the subjects showed a slight increase in serum potassium and sodium levels and elevated hematocrits. These were probably caused by transitory dehydration when the subjects did not take advantage of the automatic drinking devices. All subjects showed facial edema, injected sclera and occular discharge for 48 to 72 hours post decompression. No clinical signs of neurologic involvement were detected. All clinical laboratory values were within normal limits 72 hours after the experiment.

Of the 15 subjects used, only 2 (used in 90-second exposure tests) showed some cardiac anomaly before the experiment. Both displayed cardiac arhythmia during the baseline tests. During the actual experiment, one subject demonstrated ectopic beats, which rapidly accelerated but recovered without entering fibrillation. The other subject, however, fibrillated almost immediately at decompression and suffered cardiac arrest after 90 seconds. Subsequent autopsy revealed that a previous pathologic state involving the pericardium may have been the cause of death.

CONCLUSIONS

Perhaps the most important result of this series of tests is that all but one subject survived the experimental conditions. The fact that the chimpanzees were capable of performing a complex task and achieving a level of performance equal to or superior to their pre-exposure performance provides clear cut evidence of a functional capability not previously anticipated. At this time we may generalize that the healthy chimpanzee can survive, without apparent central nervous system damage (as measured by performance), the effects of decompression to a near vacuum up to two and a half minutes and return within approximately four hours to baseline levels of functioning. Replications of 90, 120, and 150-second exposures have added great reliability to the findings of the first series of experiments and should allow cautious extrapolation of the results to man.

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THE FRANK LEAD SYSTEM AS AN ELECTRO-PHYSIOLOGICAL MONITOR

AT 1g, 2g, AND 4g

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The electrocardiogram is generally considered a desirable parameter for monitoring human subjects in hazardous environments. In the past decade, advances in electronics plus the need to know have resulted in numerous studies in which the heart's electrical activity has been recorded under a wide range of stressful conditions. With few exceptions, however, these studies have employed single or dual channel recorders and as a rule, non-standard leads have been used. While this work has greatly enhanced our knowledge of the incidence of arrhythmias and the range of heart rate, it has provided little information as to the physiological changes in ventricular depolarization and repolarization, disturbances in intraventricular conduction, or of the incidence of myocardial ischemia. Positive identification of such changes predicates the use of a standard reference system in order to utilize the emperical knowledge, which has accumulated with the system. The relatively new orthogonal lead systems, originally introduced to obtain more accurate vectorcardiograms, provide a very satisfactory solution to the problem. Of these, the Frank lead system is, perhaps, the most suitable because of the fewer electrodes required, and extensive literature is accumulating as a result of the growing acceptance of this lead system.

This report describes the findings obtained with this lead system in healthy subjects exposed to zero g, 1g, 2g, and 4g.

PROCEDURE

All tracings were obtained on a standard three-channel ECG amplifier,[1] and recorded on a multichannel magnetic tape recorder.[2] The gain

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[1]Sanborn

[2]Ampex model FR 1300

was set for a 1-millivolt signal to provide 1 volt input into the tape recorder. The resistance (R) of the Frank network was 100K ohms. The left leg electrode was applied over the sacrum at the level of S5. The electrodes used were standard NASA types on all subjects. Skin preparation consisted of first washing with Alkanox followed by alcohol sponge. The cornified layer of the epidermis was removed with a dental bur in a high-speed drill,[1] special pains being taken to avoid weeping or scab formation. A commercially available electrode jelly[2] was employed.

The zero g flights were flown at Wright-Patterson Air Force Base, Ohio, in a modified KC135 aircraft. The flight profile consisted of the second half of the Keplerian parabola, which permitted a transition from 1g to zero g without the usual 2g insertion. The time the aircraft was in zero g averaged 10 to 12 seconds duration. Nineteen observations were made on four healthy Naval aviators who were seated in a standard aircraft seat.

The 2g and 4g observations were obtained at Pensacola, Florida, in an A1E aircraft at an altitude between 6 000 and 11 000 feet. The flight profile consisted of four 1-minute left turns, each separated by a 9-minute recovery period. Beginning at 1g in the first turn, the g was increased in each turn to 2g in the second, 3g in the third, and finally, 4g in the fourth. Altitude was held constant in the first two, but approximately 1500 and 3000 feet were lost in the 3g and 4g turns respectively. To ensure reproducibility of results the whole profile was repeated. On each of the eight exposures, a continuous recording was made from 30 seconds before the application of g until 3 minutes after its cessation. Four aviators and six student aviators were studied. The subject sat in the righ-hand seat beside the pilot in full flight gear. None of the subjects became ill or showed any outward sign of apprehension. In the 4g turn, all subjects admitted of moderate to severe grayout during the first 5 to 10 seconds of the maneuver, but none lost consciousness. Two of the subjects were flown in a 5g turn for 30 seconds.

Readout was performed on a conventional four-channel recorder.[3] Standardization was achieved by adjusting the gain of the amplifier until the previously recorded 1-millivolt standardization pulse had a 1-centimeter excursion in each channel. Skelatal muscle noise was

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[1]Handee series 6000, Chicago Wheel & Mfg. Co., Chicago, Ill.

[2]Offner Electronics, Inc., Chicago, Ill.

[3]Sanborn 964

significantly reduced with a three-stage RC low pass filter with a band pass of 0 to 50 cps and a roll-off of 60 dB per decade. Vector-cardiograms were obtained on a standard oscilloscope[1] and camera.[2] A timing pulse of 500 cps was used, resulting in a pip-to-pip time of 2 milliseconds.

The P, Q, R, S, and T waves as well as the ST segment were measured at basal conditions and during the various exposures. To avoid errors caused by beat-to-beat variation, 10 consecutive complexes were averaged for each observation. The data were punched on IBM cards and processed on an IBM 1620 computer.

The reference system used in describing the spatial forces is that suggested by Brinberg in which the azimuth corresponds to the conventional horizontal plane, the anterior half of which is positive, the posterior negative. Elevation is the angular distance of the vector from the horizontal plane. Positive angles are below, while negative angles lie above this plane.

RESULTS

Zero g flights.- The electrocardiographic changes during the 10- to 12-second exposure to weightlessness are, with the exception of heart rate, minimal. Nonetheless, they appear to be consistent and reproducible. Figure 1 shows the ECG of one of the subjects during the transition from the normal 1g environment to the weightless state. The marked reduction in rate is apparent. The increase in the T wave amplitude in X and Y is less evident. Table I summarizes the rate changes and shows the nature of the magnitude and direction of the P, QRS, and T waves. The 4 percent increase in the mean spatial QRS vector results from a 9 percent increase in the X and a 6 percent increment in the Y axis coordinates. Z remains unchanged. The T wave changes follow a somewhat different pattern. The 10 percent and 27 percent increment in the X and Y leads are counterbalanced by a 15 percent decrement in the Z axis. In consequence, there is practically no change in the amplitude of the spatial T wave. There is little or no change in the spatial heading of QRS while the T vector swings very slightly to the left and inferior. The spacial P wave also moves to the left and inferior and diminishes from 0.088 millivolt at 1g to 0.080 millivolt at zero g.

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[1]Sanborn 569A

[2]Hewlett Packard 196A

FRANK ECG IN ZERO GRAVITY

Figure 1. - On zero-g state, the most evident change is a reduction in heart rate. Less apparent is the increase in the QRS and T in X and Y axis.

TABLE I.- P, QRS, AND T WAVE CHANGES AT 1 AND ZERO g

	1g			Zero g		
	Mean	S. Dev.	Range	Mean	S. Dev.	Range
Rate	78	6.4	64/88	73	8.4	58/86
QRS						
Az	-28°	27°	-56°/7°	-29°	23	-51°/.4°
El	39°	12°	19°/52°	39°	12	21°/53°
Mag	1.16	.17	.87/1.49	1.21	.13	.97/1.39
X	.67	.16	.39/.95	.73	.17	.47/.94
Y	.70	.17	.47/.94	.74	.20	.49/1.03
Z	.43	.44	-.11/1.14	.43	.38	-.07/.96
T wave						
Az	46°	11°	32°/66°	40°	12°	24°/59°
El	23°	8°	13°/33°	28°	8°	16°/37°
Mag	.47	.07	.33/.61	.48	.05	.35/.56
X	.28	.05	.20/.34	.31	.05	.23/37
Y	.18	.05	.11/.26	.23	.06	.14/.31
Z	-.32	.11	-.54/-.20	-.28	.09	-.44/-.17
P wave						
Az	37°	12°	15°/63°	33°	17°	0°/56°
EI	57°	9°	45°/75°·	61°	8°	45°/77°
Mag	.09	.02	.04/.12	.08	.01	.05/.10

The VCG revealed subtle changes which were not apparent on statistical analysis. Figure 2 shows the opening out of the T loop in the horizontal plane which could not be anticipated from the scalar electrocardiogram.

Positive g flights.- The electrocardiographic changes at 2g and 4g are summarized in tables II, III, and IV. In general, the changes are proportional to the linear acceleration and consist of an increase in heart rate, a diminution of the spatial QRS and T-wave amplitude, and a moderate increase in the P-wave magnitude. The somewhat nominal increase in heart rate reflects the training and experience of the subjects. Despite this fact, there are significant changes at the 10-second preexposure observation. These changes are of lesser magnitude but qualitatively similar to those produced during the periods of linear acceleration.

The 4 percent and 6 percent reductions in the magnitude of the mean spatial QRS at 2g and 4g result primarily from the diminution of the X and Y components. At 4g these decline 19 and 24 percent, respectively, while the Z component increases 54 percent. These changes obviously reflect the 16° posterior and 6° superior migration of the spatial QRS vector with increasing positive acceleration. This pattern of change is applicable only for positive g forces up to and including 4g. One of two subjects exposed to 5g showed an entirely different response. As is evident on figure 3, the QRS became extremely vertical.

The spatial T wave diminishes 38 and 44 percent at 2g and 4g, respectively. With increasing positive g, the T wave also becomes more superior (13° at 4g), but unlike the QRS, becomes very slightly more anterior. In consequence, there is a widening of the spatial QRS-T angle. The spatial P wave increases 10 and 33 percent at 2g and 4g and becomes some 8° more vertical at 4g. Although these changes represent the average for all 10 subjects, they are well illustrated on figure 4, which was obtained on one of the aviators. Changes in the amplitude and orientation of QRS and T are more readily perceived in the vectorcardiogram shown on figure 5.

In addition to these average overall changes in the T wave magnitude, there were other important variations. As shown on figure 6, immediately after the 4g exposure the T wave became larger than it was in the baseline. This tracing also shows the reduction in the T wave amplitude immediately before the exposure. Figure 7 shows the variation in amplitude of the T wave during a 4g turn. The maximal reduction of T does not occur during the first 5 seconds but appears to reach its maximum at 15 seconds, after which there is a gradual recovery. By 60 seconds, the T has almost returned to its preexposure amplitude. From table III it is evident the same trend of recovery is present in all subjects.
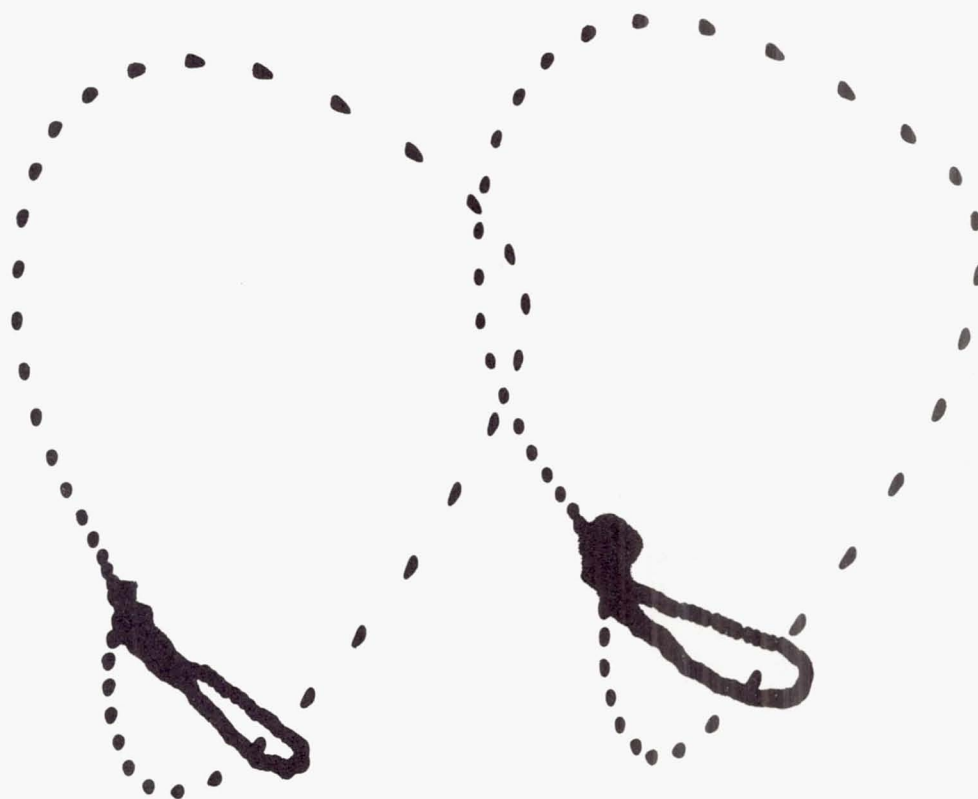
Figure 2. - Horizontal plane vectorcardiogram 1g at left, 2g right.
Note widening of T loop.

TABLE II.- QRS MEASUREMENTS ON TEN SUBJECTS AT 1g, 2g, and 4g

	1g		2g	4g					
	Base	10 sec	Average	5 sec	15 sec	30 sec	45 sec	60 sec	Average
Rate	74	90	97	120	126	124	123	121	123
SD	11.2	14.7	11.4	16.3	20.7	26.2	23.5	24.6	22.6
Range	50/92	66/130	78/122	100/146	100/158	98/164	96/162	90/162	90/164
Az	−25°	−23°	−31°	−37°	−41°	−42°	−44°	−42°	−41°
SD	14.3	15.4	17.3	17.7	17.8	15.6	16.4	17.0	17.1
R	−54/−7	−48/0	−87/−3	−65/−14	−75/−15	−73/−19	−76/−23	−77/−22	−77/−14
EL	33°	32°	30°	28°	26°	26°	27°	28°	27°
SD	11.3	10.4	10.7	1.04	10.5	10.8	11.4	10.9	10.8
R	15/55	12/51	11/46	11/45	10/42	7/41	10/47	11/45	7/47
QRS									
Mag	1.32	1.28	1.27	1.24	1.25	1.22	1.24	1.27	1.24
SD	.20	.20	.25	.30	.30	.30	.33	.31	.31
R	.99/1.7	.95/1.6	.89/1.7	.71/1.7	.85/1.8	.85/1.9	.85/1.9	.88/1.9	.71/1.9
X	.95	.94	.88	.82	.79	.76	.73	.77	.77
SD	.27	.23	.31	.32	.33	.26	.30	.30	.30
R	.47/1.5	.63/1.4	.07/1.5	.43/1.5	.28/1.3	.31/1.2	.26/1.2	.24/1.2	.24/1.5
Y	.71	.67	.61	.55	.52	.51	.55	.56	.54
SD	.23	.21	.20	.16	.19	.22	.19	.18	.19
R	.41/1.2	.33/1.1	.30/.98	.31/.87	.27/.92	.15/.97	.23/.89	.27/.91	.15/.97
Z	.46	.42	.54	.65	.71	.72	.75	.73	.71
SD	.24	.29	.32	.36	.36	.36	.37	.37	.37
R	.10/.96	−.01/1.1	.05/1.5	.14/1.5	.37/1.6	.38/1.6	.35/1.7	.34/1.6	.14/1.7

TABLE III.- T WAVE MEASUREMENTS ON TEN SUBJECTS AT 1g, 2g and 4g

	1g		2g	4 g					
	Base	10 sec	Average	5 sec	15 sec	30 sec	45 sec	60 sec	Average
Az	35°	39°	39°	26°	42°	39°	43°	43°	39°
SD	12.6	13.3	16.0	42.2	15.4	17.8	14.9	14.1	24.5
R	17/58	21/72	14/81	-90/79	19/71	0/71	24/75	22/68	-90/79
EL	26°	24°	19.6	14°	13°	12°	13°	14°	13°
SD	7.2	8.1	9.2	11.6	11.2	12.3	8.5	7.6	10.4
R	15/35	7/36	4/35	0/30	-3/31	-3/30	0/28	5/27	-3/31
T wave									
Mag	.45	.34	.28	.21	.22	.24	.28	.29	.25
SD	.12	.10	.09	.07	.09	.07	.06	.07	.08
R	.19/.64	.16/.53	.14/.51	.08/.3	.11/.37	1.4/.37	.15/.4	.2/.4	.08/.41
X	.32	.24	.20	.15	.15	.17	.19	.20	.17
SD	.11	.10	.10	.08	.06	.05	.06	.07	.08
R	.11/.55	.08/.43	.03/.42	0/.24	.06/.26	.08/.24	.07/.27	.09/.31	0/.3
Y	.20	.14	.10	.05	.05	.05	.06	.07	.06
SD	.08	.06	.06	.06	.05	.05	.05	.05	.05
R	.10/.30	.04/.28	.02/.25	-.03/.14	-.02/.13	-.02/.12	.0/.13	.02/.18	-.03/.18
Z	-.22	-.19	-.16	-.11	-.15	-.15	-.19	-.19	-.16
SD	.09	.06	.06	.07	.08	.08	.07	.07	.08
R	-.42/-.12	-.33/-.10	-.27/-.03	-.22/.08	-.3/-.05	-.3/0	-.32/-.1	-.34/.1	-.34/.08

TABLE IV.- P WAVE MEASUREMENTS ON TEN SUBJECTS AT 1g, 2g, and 4g

	1g		2g	4g					
	Base	10 sec	Average	5 sec	15 sec	30 sec	45 sec	60 sec	Average
Az	46°	46°	48°	46°	48°	44°	46°	46°	47°
SD	14.4	13.6	14.5	16.4	18.6	18.8	16.8	16.7	17.5
R	26/63	21/74	26/82	26/78	21/82	20/83	23/77	26/78	20/83
EL	46°	54°	52°	56°	56°	56°	55°	49°	54°
SD	9.7	10.1	10.9	13.5	12.8	11.6	11.8	12.6	12.8
R	30/63	38/75	29/73	30/77	30/72	36/74	33/74	23/66	23/77
P wave Mag	.09	.10	.10	.11	.12	.12	.12	.11	.12
SD	.03	.03	.03	.04	.04	.04	.04	.04	.04
R	.05/.14	.05/.16	.05/.17	.05/.18	.05/.20	.05/.18	.07/.18	.07/.11	.05/.20

FRANK ECG AT 5 G

15 sec.   I min. post 5 G
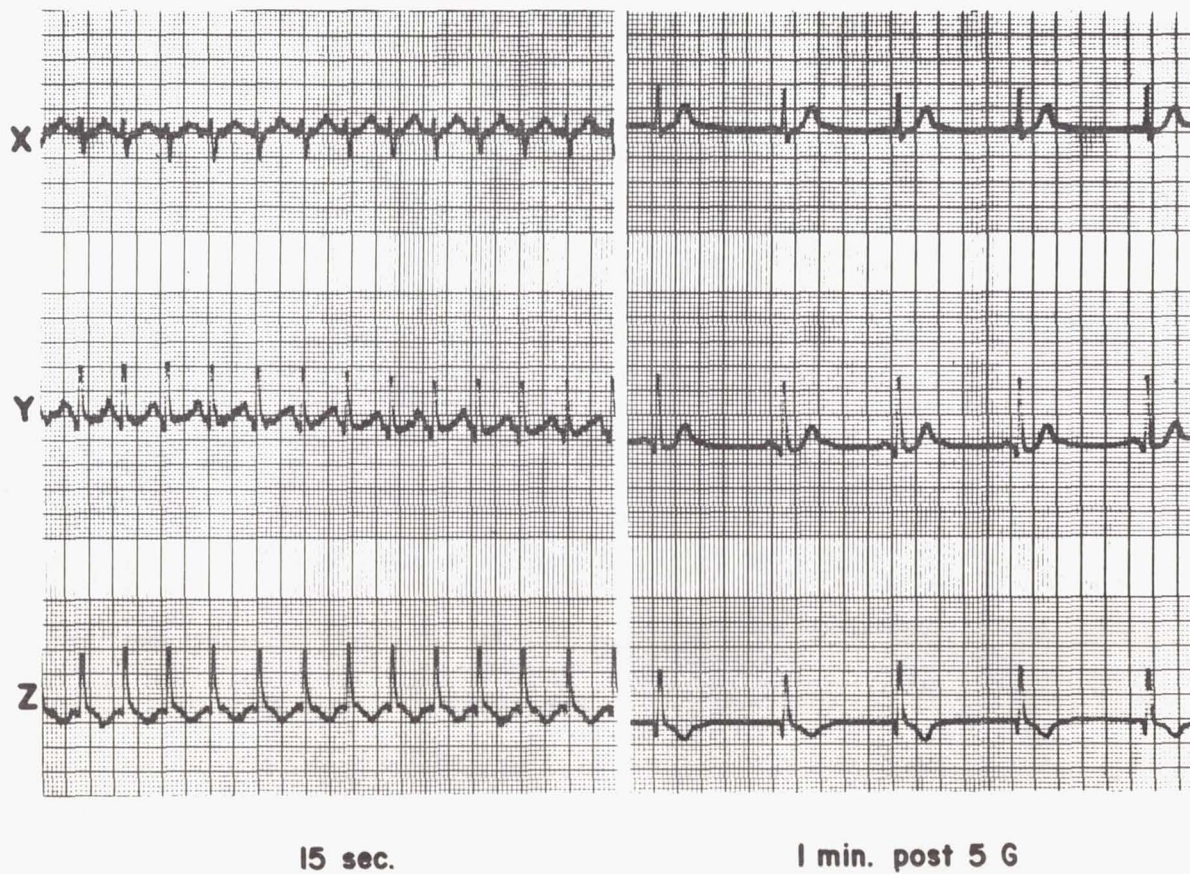
29 YR. Naval Aviator   AIE A/C

Figure 3. - The inversion of the QRS complex in the X axis was noted only at 5g.

ACUTE RESPONSE TO LINEAR ACCELERATION

28 YR. NAVAL AVIATOR   **AIE A/C**

Figure 4.- Frank ECG of 1g, 2g, 3g, and 4g.   The alteration in heart rate and T amplitude are
clearly evident.   The increase in amplitude of the QRS in the Z axis is less apparent.
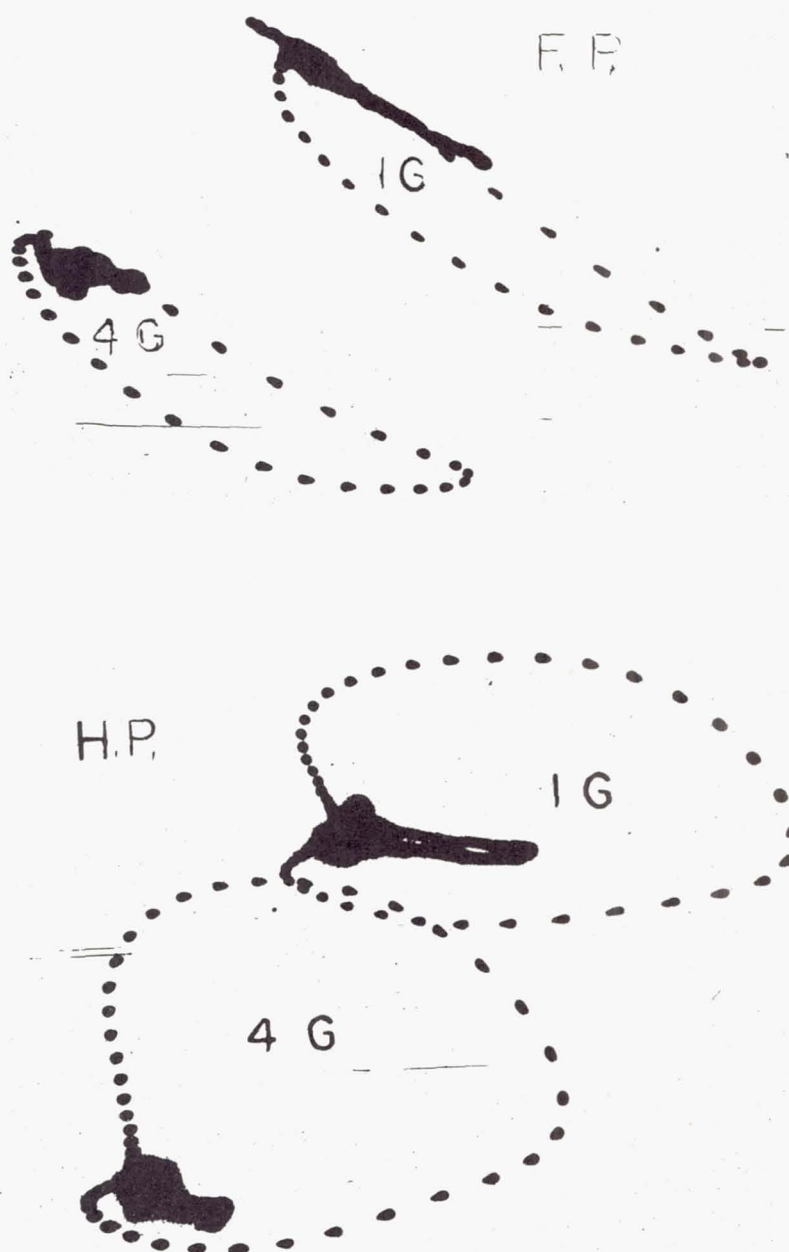
Figure 5. - Frank VCG in the frontal and horizontal planes at 1g and 4g.
The change in amplitude of QRS and T are present in both.
The posterior displacement is apparent in the horizontal plane.

VARIATIONS IN T WAVE AT 1 G

AT 10,000 FT. BEFORE G RUNS **10 SECONDS BEFORE 4 G** **10 SECONDS AFTER 4 G**
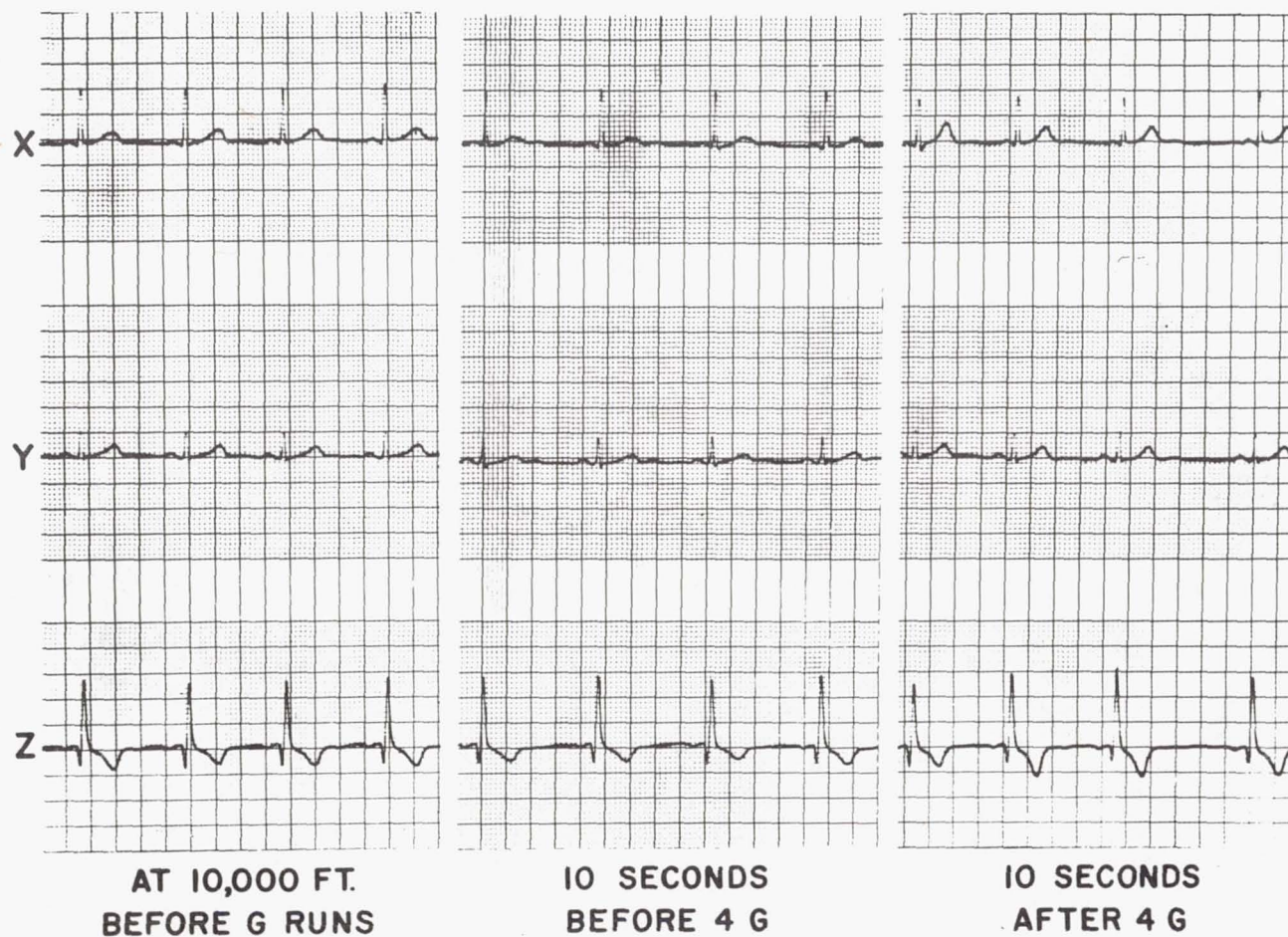
Figure 6. - Variation in the T wave at 1g. Note reduction of T just prior to g exposure. Immediately after the 4g exposure it becomes temporarily larger than in the baseline.

FRANK ECG DURING 4 G TURN

X

Y

Z

Pre   5 sec.   15 sec.   30 sec.   45 sec.   60 sec.
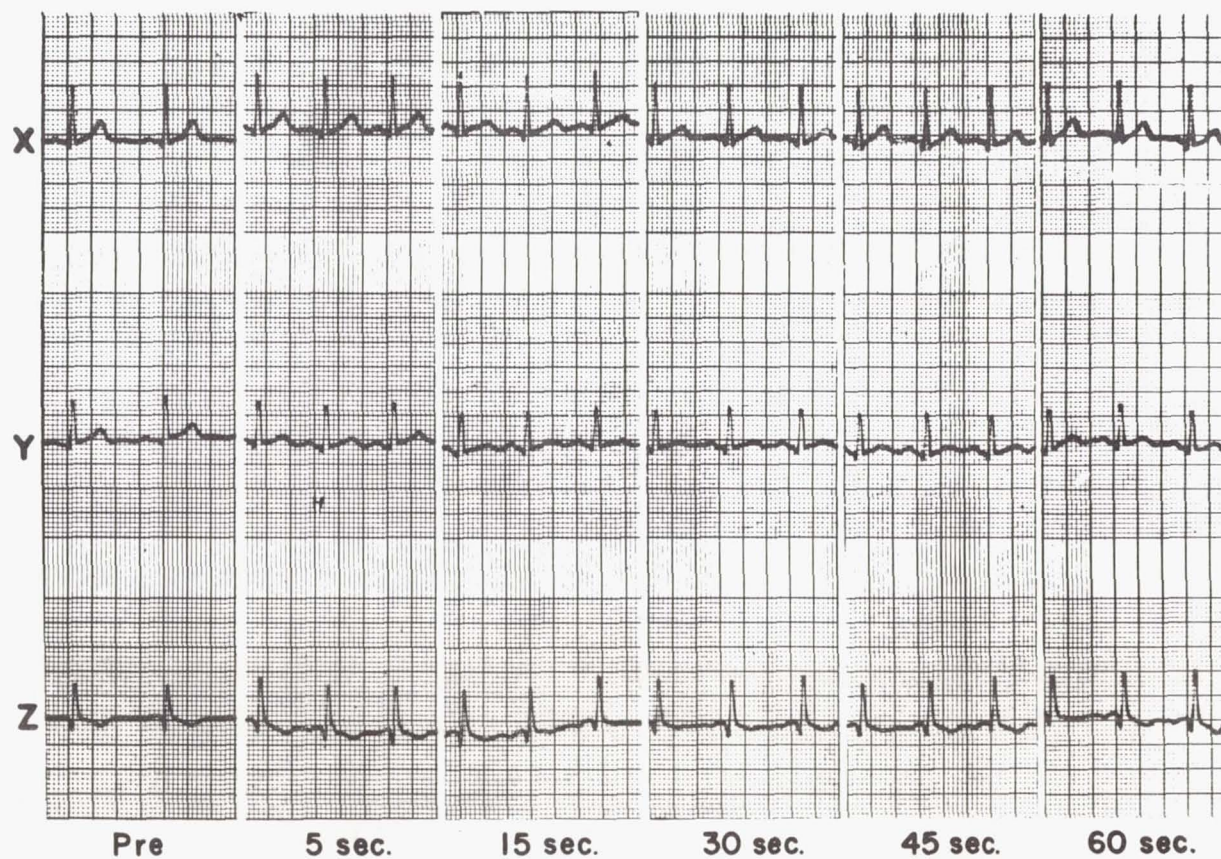
23 YR. S.N.A.   **AIE Bu. No. 135178**

Figure 7. - Tracing taken at indicated times during a 4g turn shows the delay in onset of the
T wave depression and its gradual recovery to abnormal pre-exposure amplitude.

During the whole of the recording session in only one subject did
any arrhythmia develop. This consisted of a single sinus block cycle
which occurred only twice. The first time was 30 seconds after the
first 3g run, and the second was during the second 2g exposure.

DISCUSSION

The slowing of the heart rate during weightlessness is in accord
with the findings of others. The minimal changes in the QRS and
T wave have not been previously commented upon, probably because of
differences in recording techniques. It seems likely that the most
significant cause of the QRS and T wave alteration is a change in the
physical position of the heart. Increased venous return and vagal tone
are probably also concomitantly acting factors, but presumably exert
their effect primarily on the heart rate.

The lowering of the T wave just prior to the onset of the g expo-
sure probably reflects the response of the myocardium to catecholamines
which have been shown to be released in anticipation of stressful con-
ditions. Similar T wave changes have been noted in a stress anticipation
test in which healthy subjects seated at a desk were presented with
threat of an electric shock. The complete absence of significant ST
segment changes is at variance with the experience of some, but may be
due to lower levels of g for shorter durations. Possibly it may repre-
sent a difference in interpretation. A moderate degree of J migration
occurred in six of the subjects and was of sufficient magnitude and
irregularity to render a statistical analysis of the ST segment unsatis-
factory. Changes of this sort are frequently seen after exercise in
healthy individuals and are not considered to be indicative of myocar-
dial ischemia.

The changes in the spatial orientation of the QRS forces are at
variance with the report of Bondurant and Finney, who noted no change
in this vector. The fact that these authors employed a modified Wilson
tetrahedron reference system may account for this discrepancy. The
present finding of a posterior and superior displacement of the QRS
is probably only valid to the level of 4g in most individuals because
one of the two men who were subjected to a 5g turn for 30 seconds de-
veloped a marked vertical orientation of his QRS. The widening of
the QRS-T spatial angle and diminution of the T amplitude are in
accord with the findings of others. No negative T waves were found
in the ECG of our subjects although one record contained a completely
flattened T wave in the X axis at the onset of the 4g exposure. This
change accounted for the only negative T wave azimuth in the whole series.

It is interesting to review the factors which might account for the maximal T wave flattening during prolonged positive g. The fact that there are no ischemic changes of the ST segment makes it unlikely that the T wave changes could be the result of decreased coronary perfusion. Likewise, the rapidity of its onset and the early recovery argue strongly against a hormonal etiology. Since the maximal T wave reduction occurs during the first 10 seconds and is coincident with the maximal heart rate, it is likely that changes in the tone of the autonomic nervous system are responsible for both. It has been clearly shown by Greenspan that vagal stimulation and infusion of acetylcholine result in an augumentation of the T wave with or without slowing of the heart rate. The increased amplitude in the T wave with associated slowing of the heart rate seen in most of the subjects' records immediately after the g exposure would lend support to this hypothesis.

An arrhythmia occurred in only one subject. This was a single blocked sinus cycle that occurred once during a 2g exposure and once during the second 3g recovery period. The infrequency of aberrent rhythms during positive g acceleration is in agreement with Torphy's recent report.

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EVALUATION AND DEVELOPMENT OF AN IMPEDANCE CARDIAC OUTPUT SYSTEM

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The evaluation and continued development of a system to measure cardiac output by measuring the electrical impedance changes that occur within the thoracic cage during the cardiac cycle has progressed satisfactorily. Comparison of the values obtained by the impedance method with simultaneous values obtained by the dye-dilution technique has been made on six healthy male university students. These studies involved simultaneous measurements by the two methods with the experimental subjects at rest and while they were undergoing two levels of exercise on a bicycle ergometer. The main purpose of this portion of the investigation was to compare the absolute values obtained by the two systems. The second purpose was to compare the relative changes indicated by the two methods. A third purpose was to investigate the feasibility of utilizing the first derivative of the impedance change waveform as a means to obtain the maximum slope of the impedance change waveform and to obtain the duration of ventricular ejection.

Preliminary experiments with dogs have been conducted to analyze further the source of the impedance changes observed during the cardiac cycle. An electromagnetic flowmeter was placed on the left pulmonary artery and recorded the pulmonary artery flow simultaneously with the impedance change, the derivative of the impedance change, the heart sounds, and the electrocardiogram.

METHODS

A four-electrode system was used for the experiments on human beings and dogs. Two strip electrodes were placed around the neck and two around the abdomen of man and animal. The outer two electrodes were spaced at least 2 centimeters away from the inner electrodes. The inner two electrodes were placed, one around the base of the neck and the second near the xiphisternal joint. The outer two electrodes were connected to a

constant current source providing a 100 000-cps sinosidial alternating current. The inner two electrodes were connected to a high-impedance input amplifier and suitable detection circuits to provide for the determination of the total impedance between the two inner electrodes and, also, for the impedance change that occurred during the cardiac cycle. The impedance change waveform was fed into a differentiator. For the experiments upon the human beings, the various outputs described as well as heart sounds and the electrocardiogram were recorded on a Sanborn pen recorder and a multichannel tape recorder. The experiments on dogs were recorded on a multichannel Visicorder.

Cardiac output was determined from the formula

$$\Delta V = \frac{\rho L^2}{Z_o^2} \Delta Z$$

ΔV = (stroke volume)

ρ = the resistivity of blood

L = the distance between the two inner electrodes

Z_o = the basic impedance between the two inner electrodes

ΔZ = the extrapolated maximum impedance change rate during systole when using the heart sounds as a measure of the duration of systole or the peak value of the first derivative of the impedance change waveform times the duration of systole as determined from the first derivative.

The value ΔZ was originally determined by extrapolating the maximum slope of the impedance change waveform from the base of the curve at the start of systole to the end of systole as indicated by the second heart sounds (fig. 1). The value ΔZ, when obtained from the first derivative waveform, was obtained as indicated on figure 2. The peak negative value of the derivative was multiplied by the various times as indicated by t_p, t_x, t_n. Finally, the average value of cardiac output per minute was determined by multiplying the value ΔV times the pulse rate.
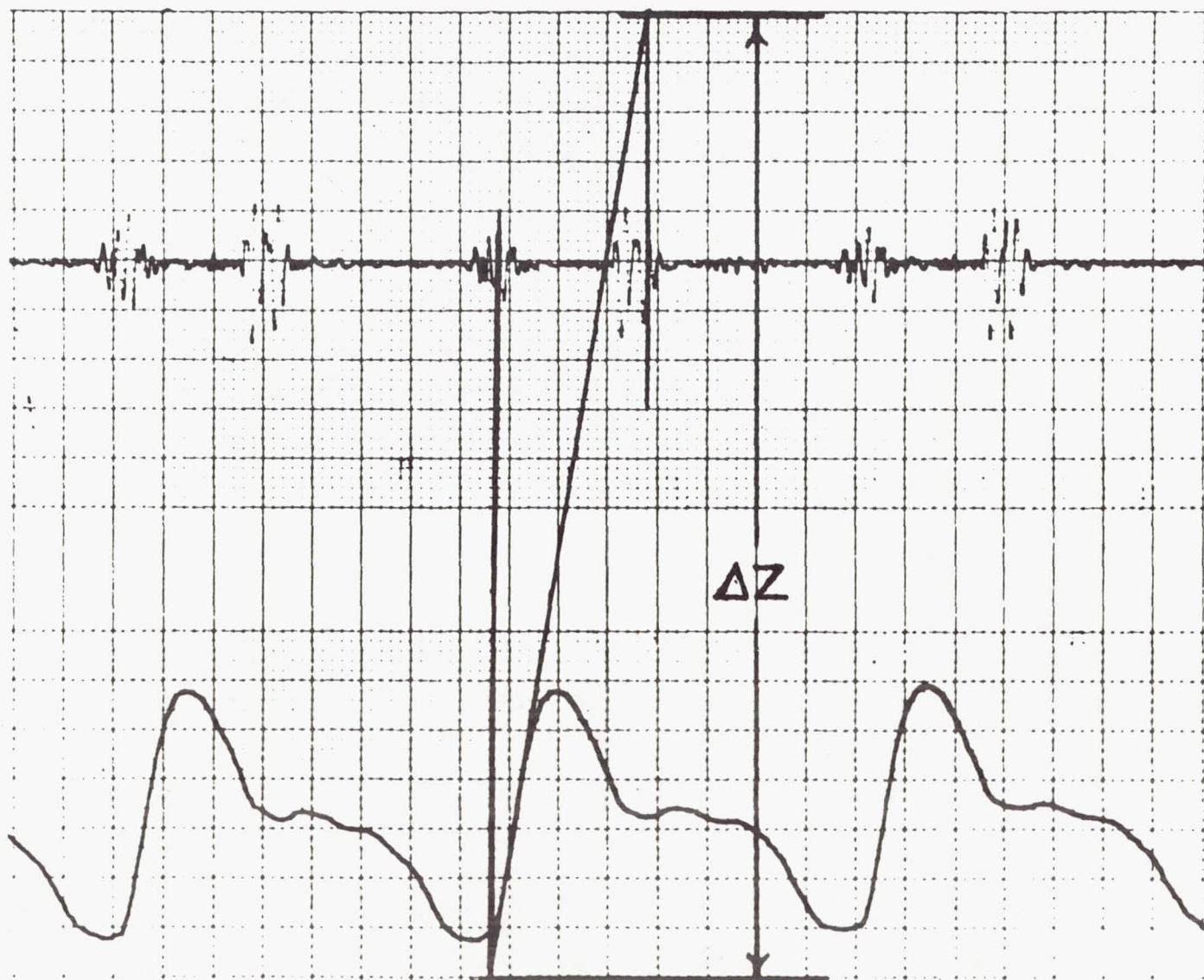
Figure 1. - Heart sounds and extrapolated impedance change (decreasing impedance upward).
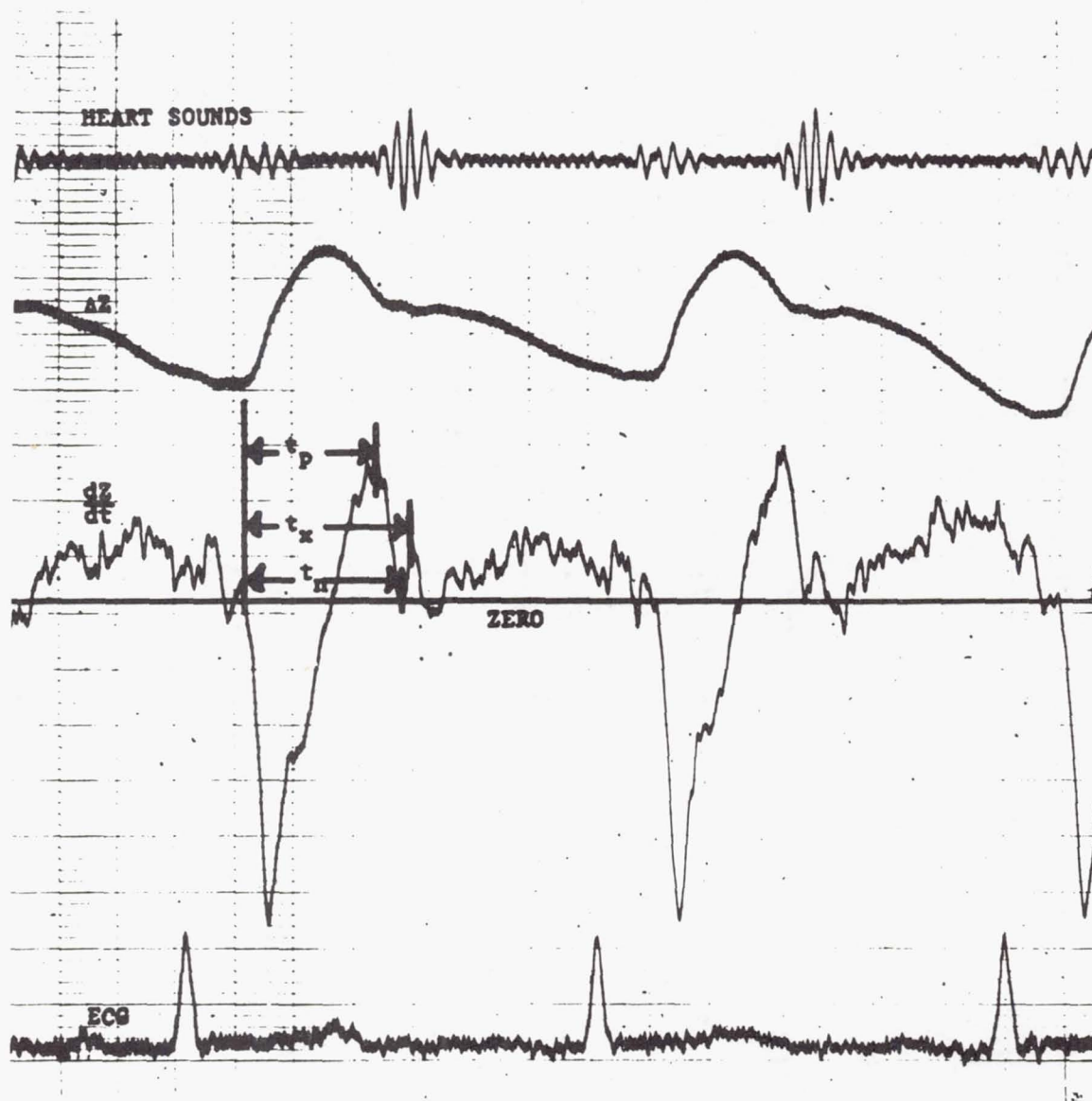
Figure 2. - Heart sounds, impedance change waveform (decreasing impedance upward), first derivative of impedance change waveform showing ventricular ejection times as described in text and ECG.

RESULTS

Figure 3 shows a graph of the dye-dilution cardiac output values versus the impedance-determined cardiac output values divided by the average ratio of the impedance value to the dye dilution value for all the subjects. For the figure, the ΔZ used in the impedance cardiac output calculation was computed by extrapolating the maximum slope of the impedance change waveform using the heart sounds for the determination of the ventricular ejection time. This impedance cardiac output is labeled Z_{S1}. The dotted lines represent 20-percent deviation lines from the solid 45-degree line. Figure 4 shows a similar graph, except that the ΔZ used in the impedance-calculated cardiac output was determined from the negative peak height of the derivative of the impedance change waveform times the time, t_p, shown on figure 2. This impedance cardiac output is labeled Z_{Kp}.

Similar graphs were constructed with the impedance-determined cardiac output calculated by using the negative peak height of the first derivative of the impedance change waveform times either t_x, t_n, as shown on figure 2, or the ventricular ejection time as determined from the heart sounds. The results of these graphs were approximately the same as shown on figures 3 and 4. However, the information required for these calculations were more difficult to obtain reliability from the graphic records.

Table I shows the ratio of the impedance cardiac Z_{S1} to the dye-dilution cardiac for each subject and each experimental condition. In the right-hand column of the table is shown the average value of the ratio for each subject. The bottom row shows the average for each experimental condition for the six subjects. The same information is shown in table II except impedance cardiac output Z_{Kp} was used.

On figure 5, the graph was constructed of the dye-dilution cardiac output versus the impedance cardiac output Z_{S1} divided by the average ratio of Z_{S1} to the dye-silution value for each subject. This average value for each subject is shown in the right-hand column of table I. The dotted lines represent 20 percent deviation lines from the solid 45-degree line. Figure 6 is similar to figure 5 except that the impedance cardiac output Z_{Kp} is used as in table II.
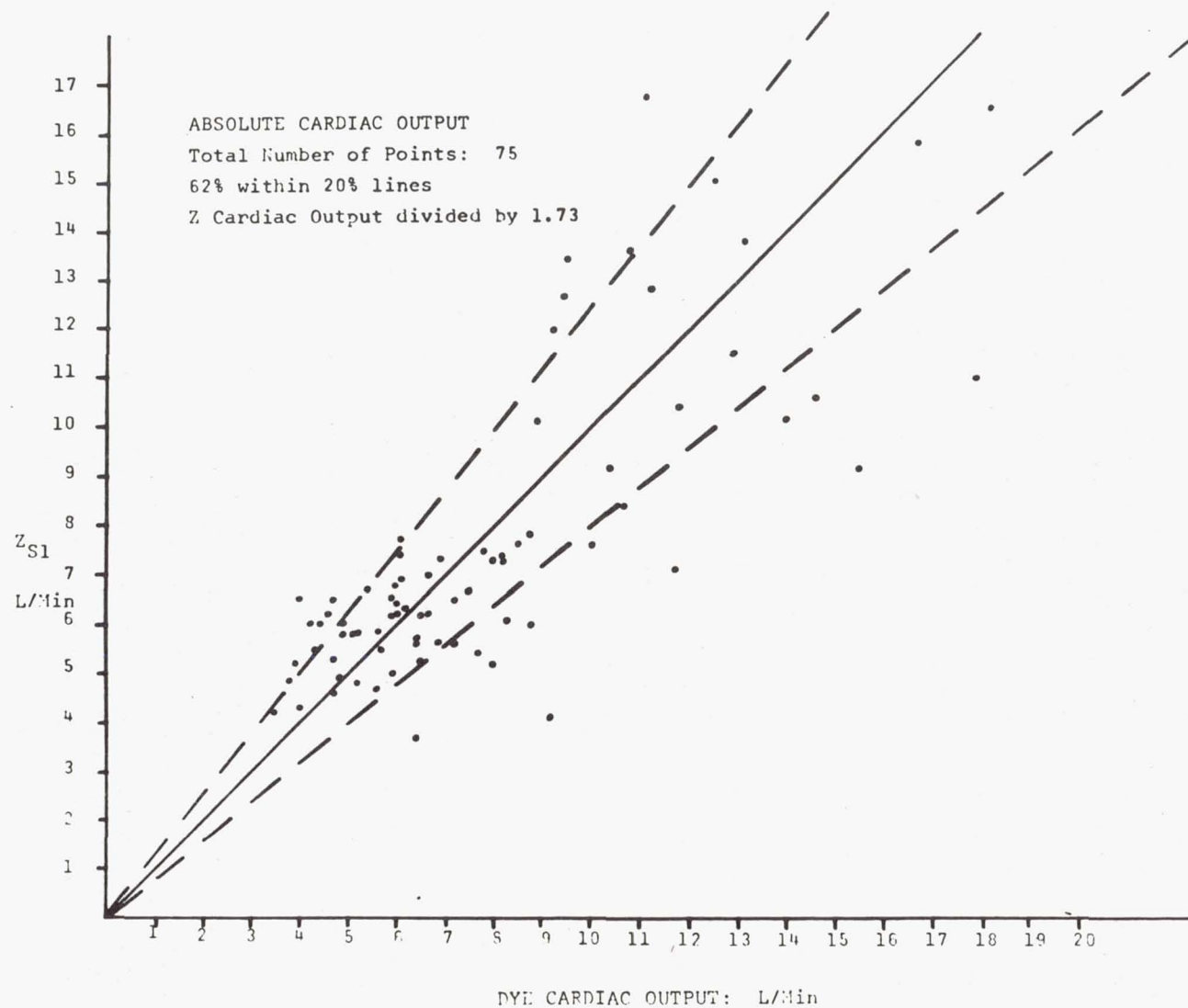
Figure 3. – Absolute cardiac output comparison for Z_{S1} (see text).
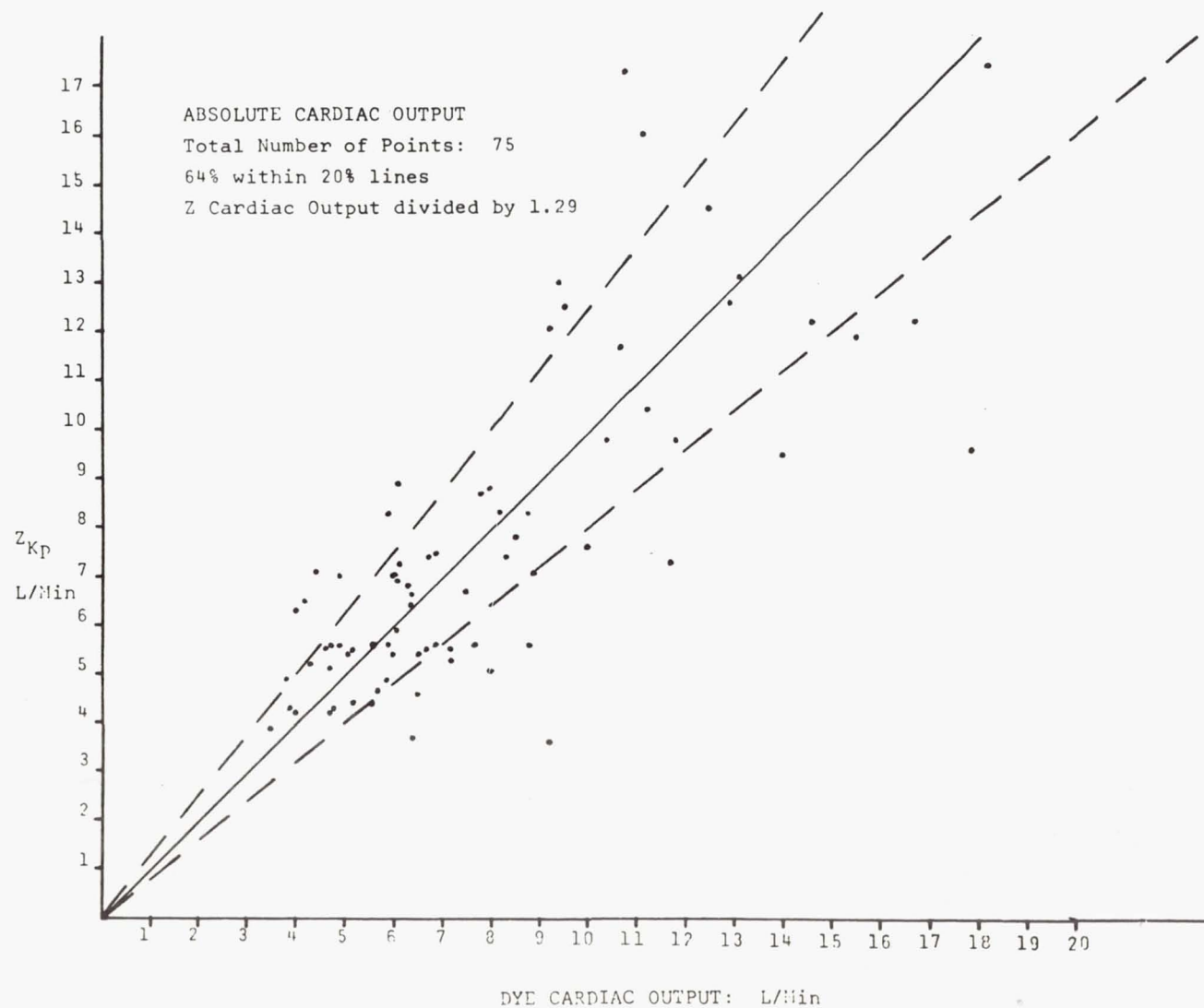
Figure 4. - Absolute cardiac output comparison for Z_{Kp} (see text).

$$\frac{Z\ CARDIAC\ OUTPUT}{DYE\ CARDIAC\ OUTPUT}\quad USING\ Z_{S1}$$

SUBJECT	SUPINE	SITTING	EXERCISE I	RECOVERY I	EXERCISE II	RECOVERY II	AVERAGE
TH	1.93	1.95	2.29	2.65	2.40	2.15	2.23
SB	.89	2.10	1.44	1.97	1.52	2.14	1.68
D6	1.62	1.78	1.39	1.84	1.55	1.91	1.68
TTH	1.41	1.60	1.18	1.57	1.86	1.42	1.51
LW	1.54	1.53					1.54
LS	1.17	1.44	1.16	1.36		1.53	1.33
JP	1.55	1.87	1.77	2.03	2.13	1.74	1.85
AVERAGE	1.44	1.75	1.54	1.90	1.89	1.81	

TABLE I. - RATIOS OF IMPEDANCE CARDIAC OUTPUT TO DYE-DILUTION CARDIAC OUTPUT FOR Z_{S1}.

$$\frac{\text{Z CARDIAC OUTPUT}}{\text{DYE CARDIAC OUTPUT}} \quad \text{USING } Z_{Kp}$$

SUBJECT	SUPINE	SITTING	EXERCISE I	RECOVERY I	EXERCISE II	RECOVERY II	AVERAGE
TH	1.77	1.69	1.75	2.02	2.03	1.50	1.79
SB	.63	1.51	.99	1.39	.91	1.44	1.14
DG	1.43	1.38	1.08	1.45	1.25	1.35	1.32
TTH	1.22	1.11	1.20	1.17	1.22	.95	1.15
LW	1.30	1.06					1.18
LS	.87	1.14	.79	.94		.98	.94
JP	1.20	1.33	1.21	1.31	1.49	1.16	1.28
AVERAGE	1.20	1.32	1.17	1.38	1.38	1.23	

TABLE II. - RATIOS OF IMPENDANCE CARDIAC OUTPUT TO DYE-DILUTION CARDIAC OUTPUT FOR Z_{Kp}.

RELATIVE CARDIAC OUTPUT
Total Number of Points: 75
84% within 20% lines

Z_{S1}

L/Min

DYE CARDIAC OUTPUT: L/Min
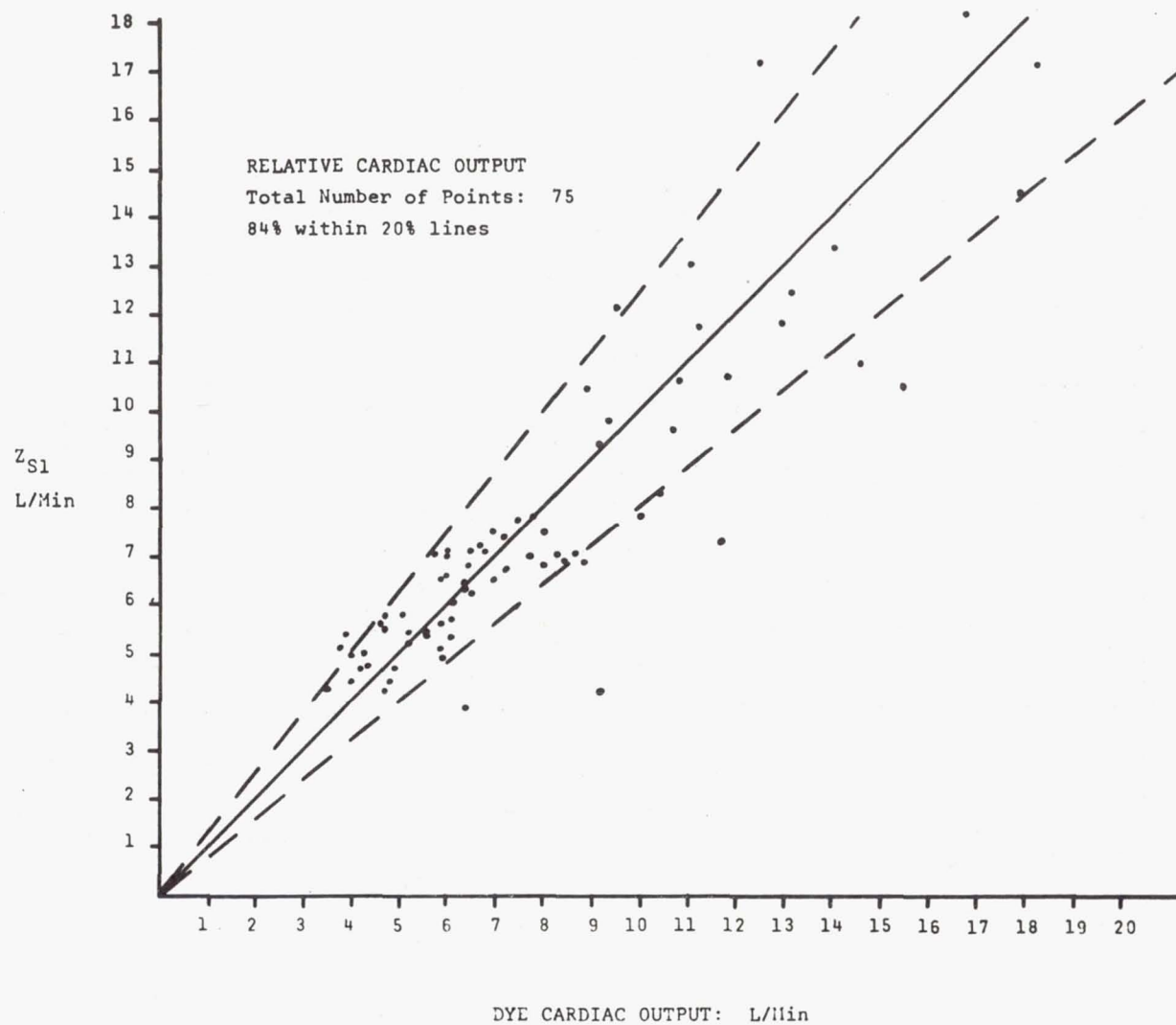
Figure 5. - Relative cardiac output comparison for Z_{S1}.

RELATIVE CARDIAC OUTPUT
Total Number of Points: 75
84% within 20% lines

Z_{Kp}

L/Min

DYE CARDIAC OUTPUT: L/Min
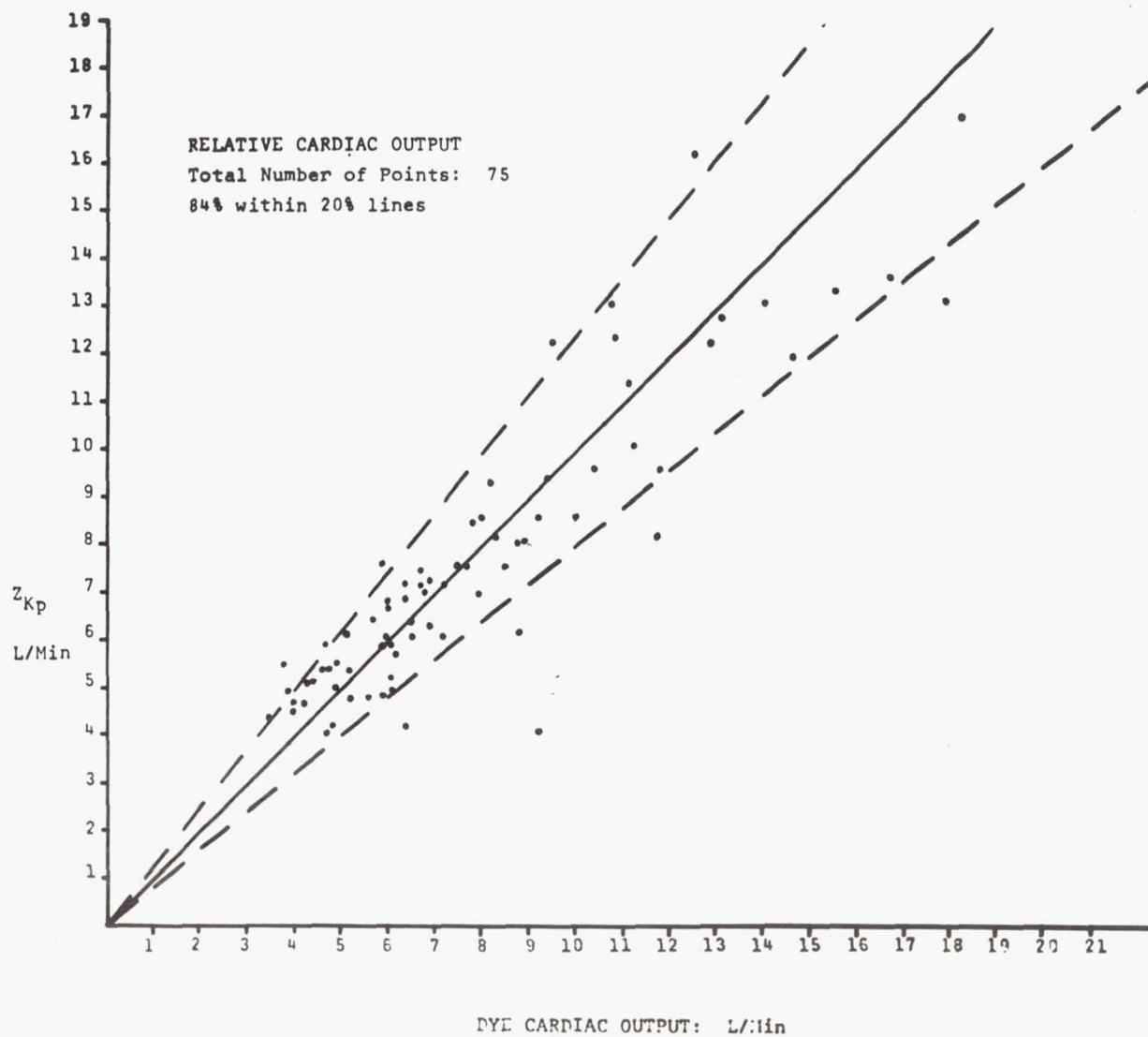
Figure 6. - Relative cardiac output comparison for Z_{Kp}.

By dividing each subject's cardiac output as determined from the impedance method by the average ratio of the impedance value to dye-dilution value for each subject, subject to subject variations tend to be reduced. Therefore, the data shown on figures 5 and 6 indicate how well the impedance-determined cardiac output indicates relative changes. The data on figures 3 and 4 indicate how well the impedance system can indicate absolute cardiac output values by using a correction factor obtained from the combined average ratios of the values from the two methods for all of the subjects.

Recordings from a pilot experiment with a dog under Nembutal anesthesia, with an electromagnetic flowmeter attached to the left pulmonary artery, are shown on figure 7. Some points of interest in this record are that the peak value of the pulmonary artery flow occurred at the time of the peak negative value of the derivative of the impedance change waveform. Also, the rather characteristic positive peak in the derivative similar to the point used for t_p, as on figure 2, occurred simultaneously with the second heart sound. Some time differences were noted between the first heart sound, the zero crossing of the derivative toward the negative peak and the onset of left pulmonary artery flow can be observed. A possible explanation may be that the time between the first heart sound and the actual start of pulmonary flow may be the time for isometric contraction of the right ventricle. Further investigation utilizing pressure recordings from the right ventricle, pulmonary artery, left ventricle, and aorta may provide a more precise explanation.

SUMMARY

The absolute values obtained by the impedance technique were in general larger than the values obtained simultaneously with the dye-dilution technique during resting and exercise conditions.

Relative changes in cardiac output, as indicated by the two methods, agreed within ±20 percent in approximately 84 percent of the values obtained thus far. In most instances the physiological interpretation regarding the response to exercise would have been identical with the data from either method.

It appears that it will be possible to utilize the first derivative of the impedance change waveform to determine the value ΔZ by multiplying the peak value of the derivative by the time for ventricular ejection as indicated by t_p (fig. 2). This would then make it possible to omit the recording of heart sounds for the calculation of cardiac output by the impedance technique.
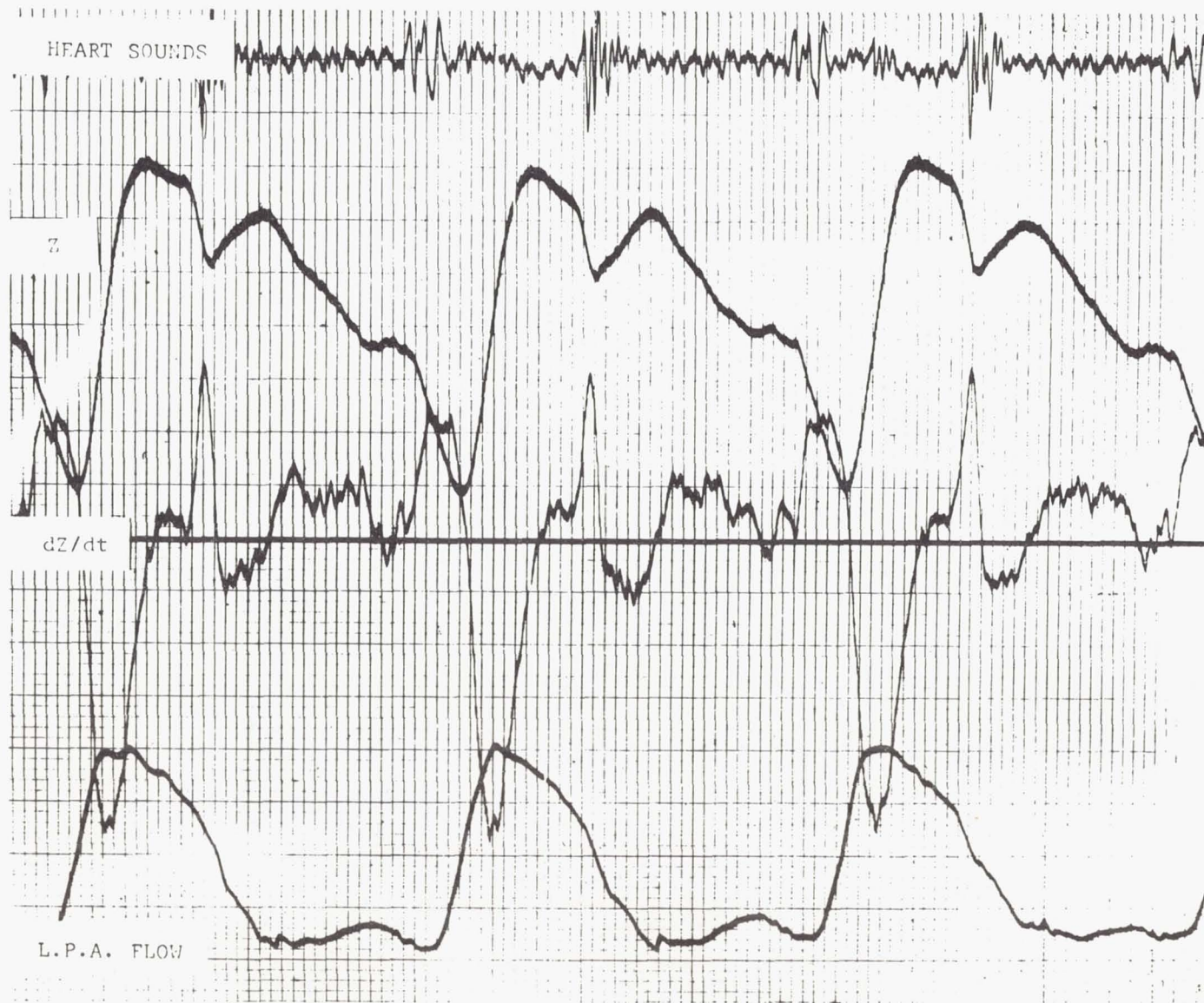
Figure 7. - Simultaneous monitoring of thoracic impedance changes, ΔZ, first derivative of the impedance change and left pulmonary artery flow (uncalibrated).

Pilot experiments on anesthetized dogs, with an electromagnetic flowmeter attached to the left pulmonary artery, confirmed the feasibility of employing the derivative of the impedance change waveform for calculating the extrapolated value ΔZ.

ANALYSIS OF BASELINE AND GEMINI VII ELECTROENCEPHALOGRAM DATA

WITH SPECIFICATION OF ON-LINE COMPUTING REQUIREMENTS

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More than ninety years ago, continuous oscillations in potential differences were first recorded across the scalp of man (Caton, 1875). These oscillations were called the electroencephalogram (EEG) by Berger (1929), who observed the broad relationship between the regularity of these waves and closing the eyes. These early findings led to enthusiastic endeavors to relate the EEG to the finer aspects of consciousness. Disillusionment followed rapidly in an era where evaluation of the records rested on visual inspection. Their inherent complexity challenged the investigator to seek evidence of their patterning through the use of increasingly sophisticated mathematical analyses (Grey Walter, 1950; Siebert et al., 1959; Burch, 1955; Adey and Walter, 1963; Walter and Adey, 1963, 1965; Adey, 1965). The power of spectral and other times series analyses (Blackman and Turkey, 1959) used in conjunction with the modern digital computer has made it feasible to test the basic interrelations between EEG patterns and specified behavioral acts, which include learned performances (Walter, Rhodes and Adey, 1965).

Nevertheless, widespread doubts have persisted that the EEG would ever be established as having a basis in the transaction and recall of information in cerebral systems, and that it, in fact, might be merely a noise therein. Moreover, the difficulties in its acquisition with older transducing techniques in inexperienced hands lent credence to the view that it would be impractical to rely on it as a physiological monitor in the aerospace environment. Developments during the past 5 years have essentially demolished these lingering shibboleths. Intracellular recording in a variety of anesthetized (Fujita, 1964) and unanesthetized (Creutzfeldt, Fuster, Lux and Nacimiento, 1965; Elul, 1965) have indicated a series of precisely definable relationships in the genesis of the EEG as a wave process at the cellular level. It can no longer be considered as a random process unrelated to the cellular transaction of information. Use of electrodes free from contact potential and making a sliding scalp contact, yet remaining artifact free, eliminated the need for adhesive or penetrating scalp contacts (Kado, Adey

and Zweizig, 1965). Using these electrodes with microminiature circuits
laid a firm foundation for the direct monitoring of central nervous
activity as a highly meaningful measure of the behavioral state.

With seemingly endless individual variations in EEG patterns, we
have established a common baseline of astronaut candidates. This common
baseline is not merely in broad shifts of consciousness but in the per-
formance of vigilance tasks and discriminative visual performances that
simulate closely the conditions of critical judgment requirements for
aerospace flight. Subsequent application of pattern recognition tech-
niques to these initial spectral analyses have allowed computer recog-
nition of inter- and intrasubject factors. These factors delineate
these states of consciousness with precision and use minimal numbers of
EEG channels and a small number of variables within each channel (Walter,
Rhodes and Adey, 1965). On this basis, it becomes feasible to specify
the requirements for on-line computer analysis of the EEG with display
techniques suited to the medical monitor or with an in-flight computer
to the needs of a pilot warning system.

Applications of the basic analysis techniques to EEG data from an
astronaut in states of sleep and wakefulness during the flight of
Gemini VII will be described.

ESSENTIAL NATURE OF THE ELECTROENCEPHALOGRAM - ITS CELLULAR ORIGINS

Intracellular recording in unanesthetized cortical neurons in our
laboratory (Elul, 1965; Adey and Elul, 1965) revealed a large wave pro-
cess (5 to 15 millivolts in amplitude) which appears to arise in the
dendritic branches of the cell rather than in the soma (see fig. 1).
Spectral analysis of this wave process has indicated that its density
distribution closely follows that of the EEG recorded grossly in the
same domain of tissue. Despite this similarity of density contours,
calculations of coherence (Walter, 1963) between the intracellular and
gross EEG records have shown that there is, virtually, no linear re-
lationship between the two processes. The population of neuronal gen-
erators appear to be independent and non-linearly related (Elul, 1965).
The wave process recorded extracellularly arises from generators no
larger than cellular dimensions (Elul, 1962), and has an amplitude less
than one hundredth of the intracellular wave process. Elul has sug-
gested that the occurrence of a rhythmic EEG as the integral of activity
in such a population of independent and non-linearly related generators
may be mathematically modeled in terms of the central limit theorem of
Cramer (1955).

NEURONAL WAVES

A.

EEG

INTRACELL.

⌶ 100 μV

⌶ 50 mV

├──────┤ 250 msec

B.

C.
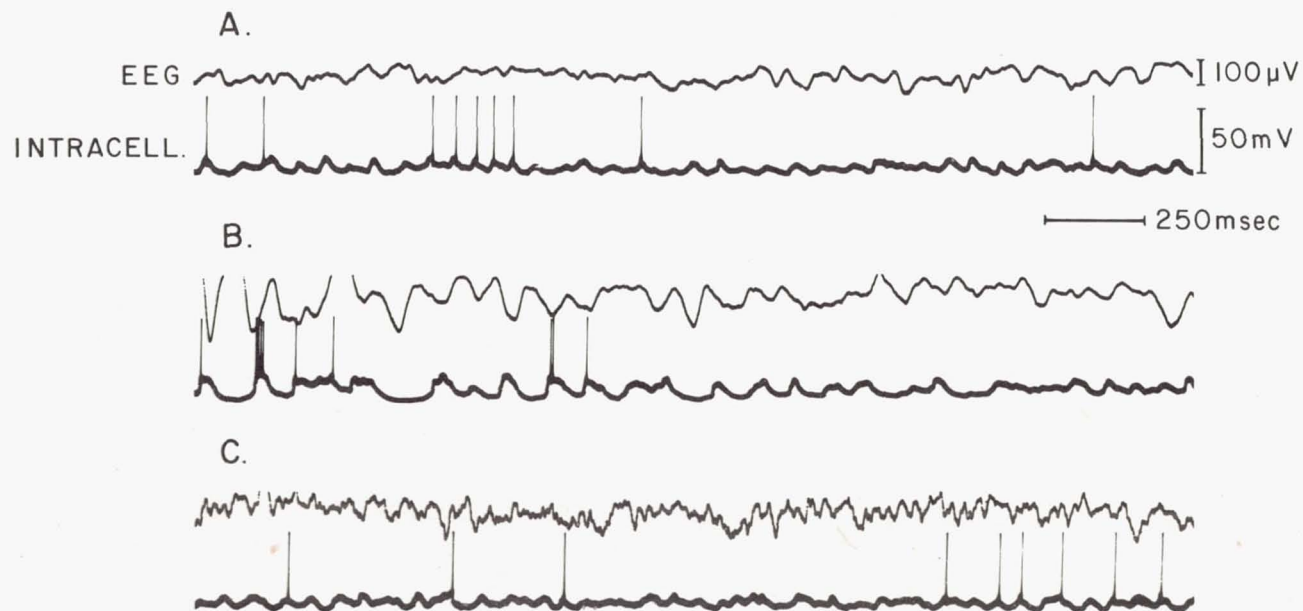
Figure 1. - Analysis of baseline and Gemini GT-7 flight EEG data in specification of on-line computing requirements.

This cellular origin strongly suggests a vital relationship to the transaction of information in cerebral tissue not only for the broad aspects of sleep and wakefulness but also for the fine processes of focused attention and discriminative judgment. This hypotesis is borne out in the normative library from 50 astronaut candidates.

SPECTRAL METHODS OF ANALYSIS - EVALUATION OF FINELY SHIFTING POWER DISTRIBUTIONS AND COMPONENTS SHARED BETWEEN CHANNELS

The EEG represents an essentially continuous spectrum of frequencies from less than 1 cycle per second to more than 50 cycles per second. Functions relating intensity to frequency in any one lead are classified as autospectra, and cross-spectra describe shared intensities across a band of frequencies (Walter, 1963). Both analog and digital spectral analyses were applied to EEG records. Problems of designing physical filters with narrow skirt characteristics led to the development of digital filters, which the digital computer provides the weighing factors for multiplying the time function. The sum of these products is taken as the output of the digital filter. The weighing function can be considered as having a narrow passband characteristic, as an analog filter, or the application of a set of digital filters to a function of time can be viewed as a discrete version of a Fourier transform (Walter, 1963; Adey, 1965).

It is in our capacity to specify precisely the bandpass characteristics of the digital filter in the low frequency range between 0.5 and 10 cycles per second, that established its superiority over analog methods. Because its phase shift is zero, it is possible to measure for the first time the phase relations between two EEG wave trains at each frequency across the spectrum as well as the shared amplitudes at each frequency. This led us to the calculation of the coherence function as a measure of statistical variability in linear interrelationships between brain regions. Its magnitude may be expressed:

$$coh(f) = MAGS(f)/ASX(f) \; ASY(f)$$

where $MAGS(f)$ is the mean cross spectral magnitude at frequency f and $ASX(f)$ is the autospectrum of X and $ASY(f)$ the autospectrum of Y, at the respective frequencies. The coherence function is expressed between 0 and 1 and is a measure of the linear predictability of activity in any area on the basis of knowing the activity in any other area or series of other areas. It is a most valuable measure of changing brain organization in focused attention, emotional arousal, fatigue and sleep, even with minimal numbers of channels for comparison, as was shown during the recent flight of Gemini VII.

DEVELOPMENT OF SIMPLE PATTERN RECOGNITION TECHNIQUES
BASED ON DISCRIMINANT ANALYSIS

Use of the spectral analysis methods has allowed the recognition of patterns in the EEG, because of the ability to compress on a single contour plot many minutes or several hours of raw records. At the same time all relevant details that may be transient and last but a few seconds will be retained (Walter and Adey, 1965; Adey, 1965).

Such plots are too complex for easy use by the flight monitor, however, and have caused the development of simple pattern recognition techniques with discriminant analysis (Walter, Rhodes and Adey, 1965). Using typical matrix methods, it has been possible to secure a computed classification of the variables that specify states ranging from wakefulness through the EEG correlates of vigilant task performance to the detection of differences accompanying progressively more brief and difficult visual discriminations. The method was applied to data from a series of subjects simultaneously as well as to their individual records.

This method was applied to the outputs of the initial spectral analyses, and the method indicates the feasibility of a reliable recognition technique and the compatibility with on-line analysis. At this stage, particular value has rested in directing attention to the small numbers of data channels and variables which reliable decision making may be determined. Moreover, the method requires short epochs of data, probably as little as 30 seconds.

APPLICATIONS IN BASELINE ANALYSIS - THE NORMATIVE EEG LIBRARY

It has long been a matter of concern that definition of EEG patterns has rested not only on the subjective opinion of the investigator, but also, on wide individual variations in apparently normal subjects. We sought to establish by computer analysis the presence of common EEG factors in a significant number of astronaut candidates in relation to task performances and assessment of sleep states.

In detailed studies (Walter-Rhodes, Kado and Adey, 1966) 200 astronaut candidates were tested in a series of perceptual and learning tasks by means of a programming device. This programming device was developed in our laboratory and used a magnetic tape command system to ensure accurate timing in task presentation from one subject to the next. Subject testing and EEG recording were performed by Doctors P. Kellaway and R. Maulsby in the Methodist Hospital at Houston, Texas. Physiological
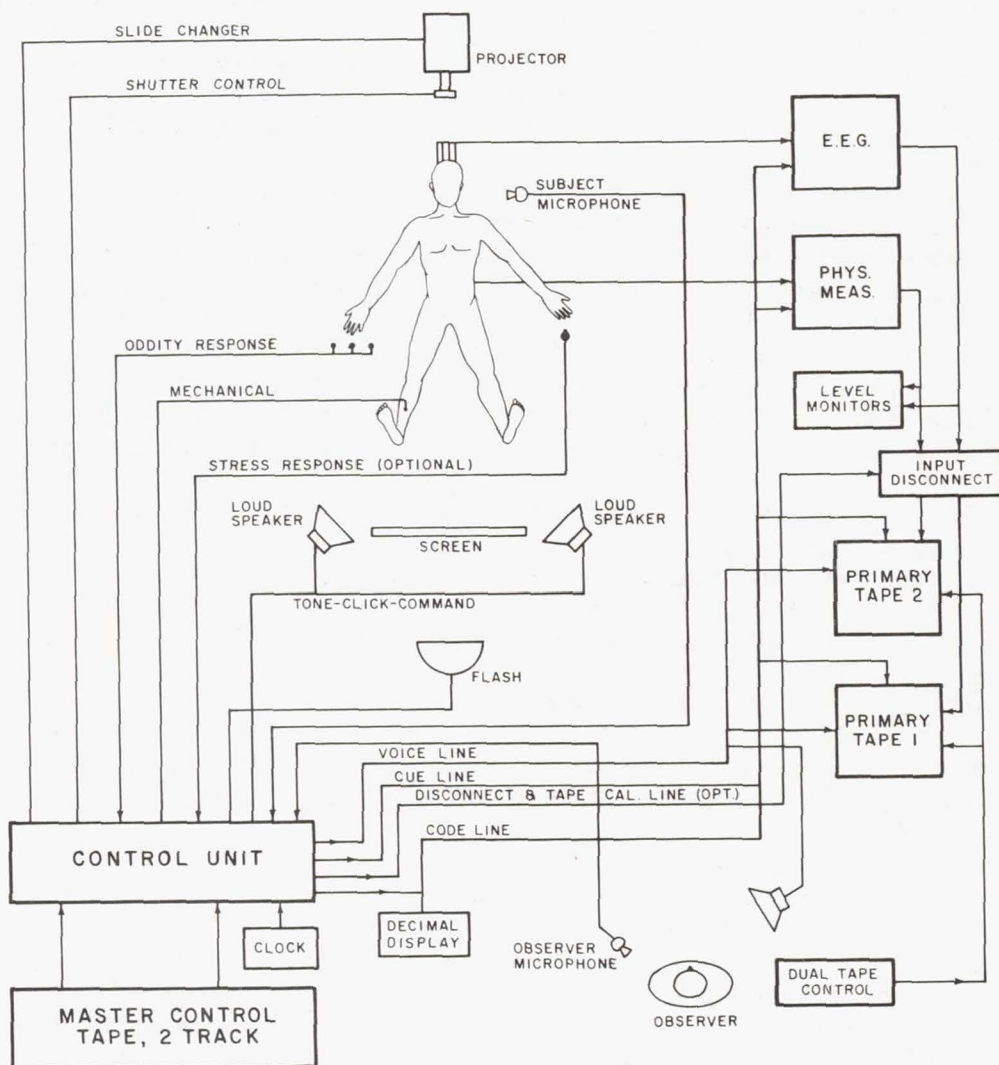
PSYCHO-PHYSIOLOGICAL TESTING AND
DATA ACQUISITION SYSTEM BLOCK DIAGRAM

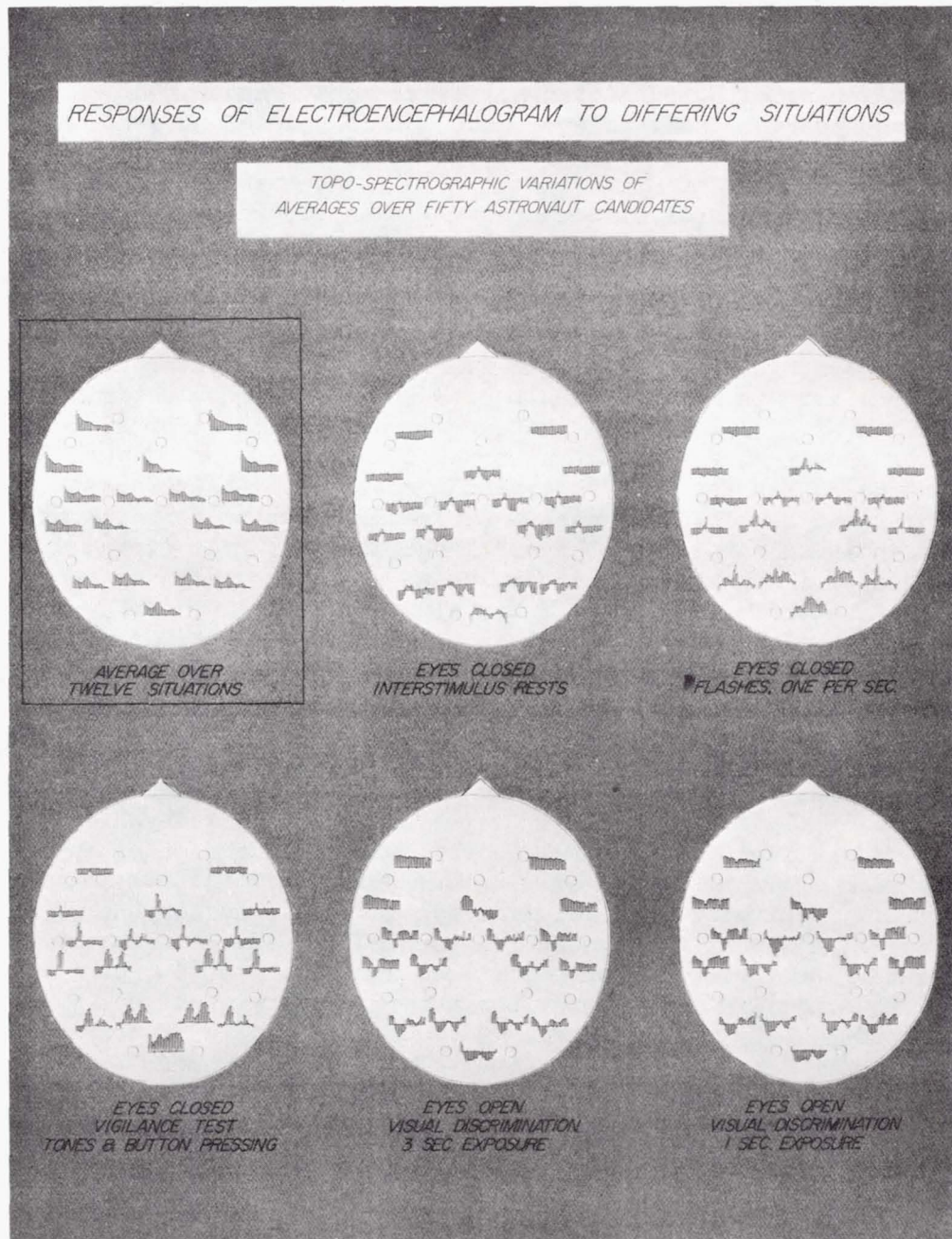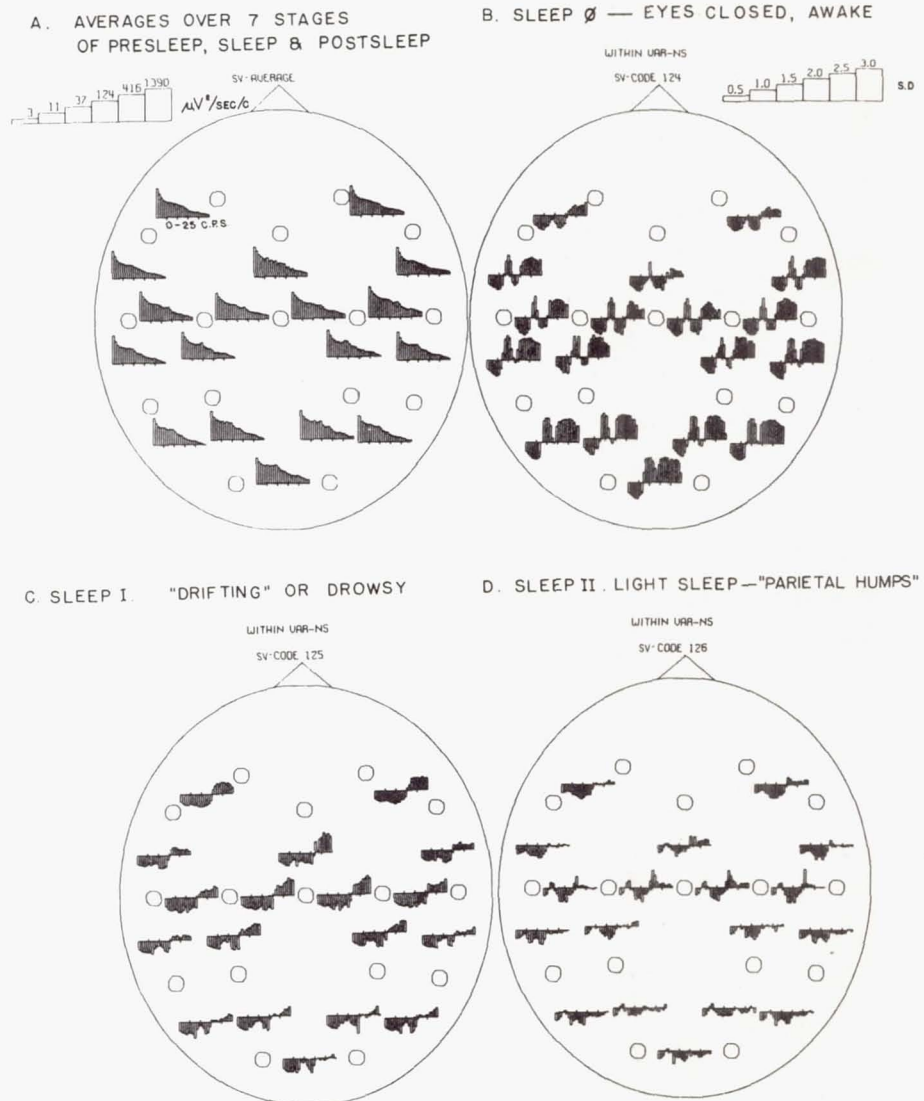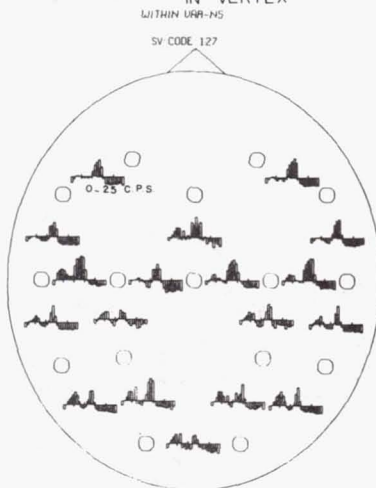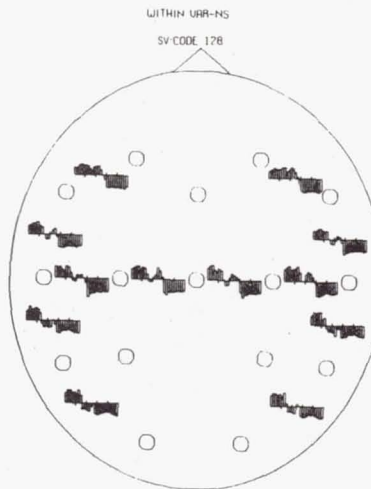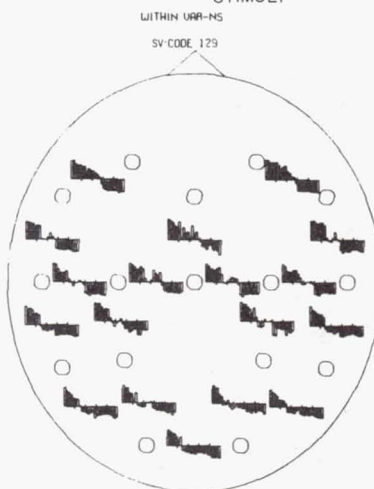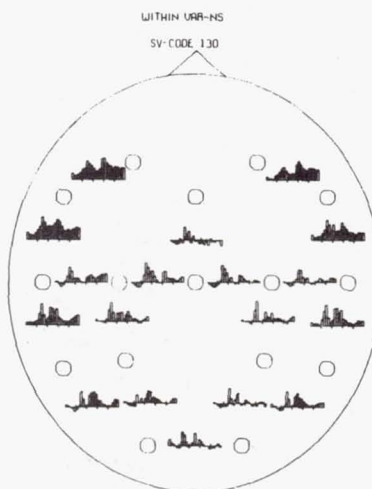Figure 2. - Analysis of baseline and Gemini GT-7 flight EEG data in specification of
on-line computing requirements.

data and command signals were recorded on magnetic tape for computer analysis. This data constitutes a normative library and includes 18 EEG channels from all scalp areas but, also, the electrooculogram (EOG), electrocardiogram (EKG), galvanic skin responses (GSR), and respiration channels.

A series of 50 subjects were selected at random from 200 and intensive spectral analyses were made. Each hour of subject data required 25 hours of main computation time. During computation time, multiplications were made at approximately 500 000 per second, which indicates the scope of the analysis. Moreover, this comprehensive analysis appears to be well justified because it allowed selection of variables for a possible on-line system that would be far less demanding in computer requirements.

To synthesize the data, an averaging procedure was adopted on the spectral outputs for all 50 subjects in the various test situations and in selected sleep epochs. These averages were made for each scalp region and are presented as a series of bar graphs on figure 3. The spectrum is between 0 to 25 cycles per second. An average was prepared of spectral densities at each scalp recording site for all test epochs. This included sitting with eyes closed at rest, eyes closed during one-per-second flash stimuli and during an auditory vigilance task and visual discriminations at 3 second intervals, and a similar series of more difficult discriminations at 1-second intervals (see the top left of fig. 3).

The contours of these "lumped" spectra were used as the means for comparison with the spectra for the individual situations. The subsequent graphs on figure 3 show the variations about the mean that was established by the average of twelve situations displayed on the top left of the figure. Spectral densities above the mean at any frequency have bars above the baseline and vice versa. It will be seen that such a display separates spectral density distributions for the 50 subjects in the five situations shown. In particular, the distributions for more difficult visual discriminations during 1 second (lower right of fig. 3) exemplify trends that characterize discriminations made during 3 seconds (lower middle of fig. 3). It is possible to compare an individual with the mean for the group or with his own mean by using a two-color display technique.

Similar averages were made for 30 subjects during their various stages of sleep and drowsiness (see figs. 4 and 5). The mean was established by an average of seven stages of presleep, sleep, and postsleep, and thus the mean became the baseline for measurement of variance for individual sleep states. It will be noted that the states of drowsiness,

Figure 3. - Analysis of baseline and Gemini GT-7 flight EEG data in specification of on-line computing requirements.

ELECTROENCEPHALOGRAPHIC CHARACTERISTICS OF SLEEP

TOPOSPECTROGRAPHIC VARIATIONS OF AVERAGES OVER 30 ASTRONAUT
CANDIDATES

A. AVERAGES OVER 7 STAGES
OF PRESLEEP, SLEEP & POSTSLEEP

B. SLEEP Ø — EYES CLOSED, AWAKE

C. SLEEP I. "DRIFTING" OR DROWSY

D. SLEEP II. LIGHT SLEEP —"PARIETAL HUMPS"

Figure 4. - Analysis of baseline and Gemini GT-7 flight EEG data in specification of
on-line computing requirements.

ELECTROENCEPHALOGRAPHIC CHARACTERISTICS OF SLEEP

TOPOSPECTROGRAPHIC VARIATIONS OF AVERAGES OVER 30 ASTRONAUT CANDIDATES

E. MEDIUM SLEEP — 14/SEC SPINDLES IN VERTEX

WITHIN VAR-NS

SV-CODE 127

F. DEEP SLEEP — HIGH VOLTAGE SLOW WAVES

WITHIN VAR-NS

SV-CODE 128

0 - 25 C.P.S.

G. SUB-AROUSAL — "K-COMPLEX" TO AUDITORY STIMULI

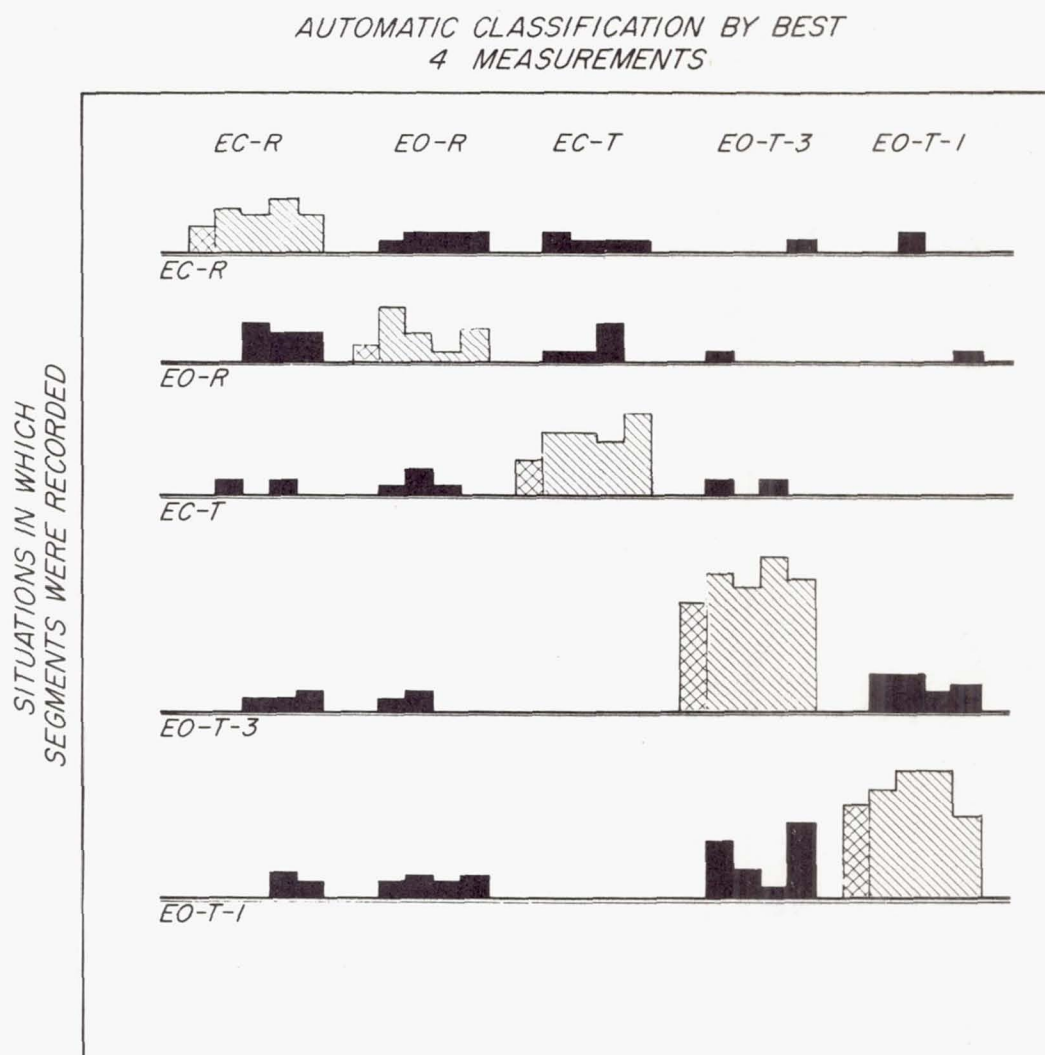WITHIN VAR-NS

SV-CODE 129

H. AROUSAL TO AUDITORY STIMULI

WITHIN VAR-NS

SV-CODE 130

Figure 5. - Analysis of baseline and Gemini GT-7 flight EEG data in specification of
on-line computing requirements.

and light, medium, and deep sleep can be readily distinguished but
that separation of deep "slow wave" sleep from subarousal with
"K-complexes" is less apparent.

Discriminant analysis was applied to these spectral outputs of
four subjects (Walter-Rhodes and Adey, 1965) for five situations, which
were eyes closed at rest, eyes open at rest, an auditory vigilance task,
and the two visual discriminative tasks. A computer program attempted
to assign each segment to the situation from which it came and used
measurements derived from four EEG channels, which were left and right
parieto-occipital (P3 - 01 and P4 - 02), vertex (FZ-CZ), and bioccipital
(01-02). Each channel's activity was analyzed into four frequency bands
and were 1.5 to 3.5 cycles per second (delta band), 3.5 to 7.5 cycles
per second (theta band), 7.5 to 12.5 cycles per second (alpha band),
and 12.5 to 25 cycles per second (beta band). For each band, measure-
ments were made of the strength of activity in each channel, mean fre-
quency within the band (the dominant frequency when present), band width
within the band (an expression of the regularity of the dominant fre-
quency), and the coherence between pairs of channels.

This discriminant analysis program initially considers all the
measurements for all the segments and selects the parameter that dis-
criminates segments recorded in different situations. It then reexam-
ines all measurements and chooses the parameter which will add most to
the discriminating power of the first measurement. It calculates five
linear functions of those two measurements whose values differ as much
as possible among the situations. The program continues this iteration
of selecting and calculating linear functions, until insufficient im-
provement is made by adding another parameter.

The four variables that best distinguish the five situations are:
left parieto-occipital alpha intensity, the mean frequency of theta-
band activity in the vertex, the coherence in the theta band between
left parieto-occipital and vertex, and coherence in the beta band be-
tween vertex and bioccipital leads. A detailed account of the respective
contributions of each of these variables to the identification of each
of these situations is given elsewhere (see Walter, Rhodes and Adey,
1965).

The separate analysis of each subject's records in the same way
yielded a higher proportion of correct classifications than in the group
analysis. With his four best measurements, between 62 and 69 percent
of a single subject's samples were classified correctly, as contrasted
with 51 percent for the subjects simultaneously. An even greater dis-
parity appeared after fifteen measurements were selected. Individually,
95, 93, 96, and 90 percent were correct, while for the subjects together,

only 65 percent were correct (fig. 6). It would appear that each sub-
ject may have a spatially and numerically characterized individual EEG
"signature," as to which measurements are most effective in distinguish-
ing different situations.

REQUIREMENTS FOR ON-LINE COMPUTATION

On-line analysis of EEG records for classification of behavioral
state would appear a desirable objective from the point of view of the
medical monitor, or for pilot warning in anticipation of defective at-
tention through drowsiness, fatigue, or problems of environmental support.

The elaborate computer system for methods of analysis has been
described (see fig. 7). Such a comprehensive analysis appears to be
justified because it allowed successful evaluation of EEG patterns within
and between a population of astronaut candidates. And hopefully, the
analysis has established a baseline for use in future flight studies.
It has also indicated the feasibility of using a small, special-purpose
computer that would work with data from three or four EEG channels. The
small, special-purpose computer could achieve a classification of state
on the basis of calculations of a small number of variables for each
channel, which would include spectral densities and band widths, domin-
ant frequencies and coherence functions. Such requirements would appear
within the current state of the computer art. Such a system (developed
theoretically by D.O.W.) would have a flight computer calculating spec-
tral characteristics and applying weighting factors to these calculations
for classification of state (see fig. 8). Only a limited amount of data
would be telemetered to a larger flight monitoring computer program.

APPLICATION OF THESE ANALYSIS TECHNIQUES TO FLIGHT EEG DATA
FROM GEMINI VII - PRELIMINARY EVALUATION

Successful EEG recording from Astronaut Frank Borman for a period
of 54 hours during the initial phase of the Gemini VII flight provided
the first opportunity to evaluate these baseline techniques for flight
monitoring. For the first 30 hours two channels of data were recorded.
After 30 hours of flight one channel of data was recorded. As will be
indicated, one channel provided highly significant data on sleep and
wakefulness. The flight data was available to us for 2 weeks prior to
this meeting, and all data were analyzed but comprehensive displays for
the whole period of 54 hours are not complete.

Figure 6. - Analysis of baseline and Gemini GT-7 flight EEG data in specification of on-line computing requirements.

COMPUTER-ASSISTED ASTRONAUT MONITORING METHOD

I. Comprehensive Data Collection Phase
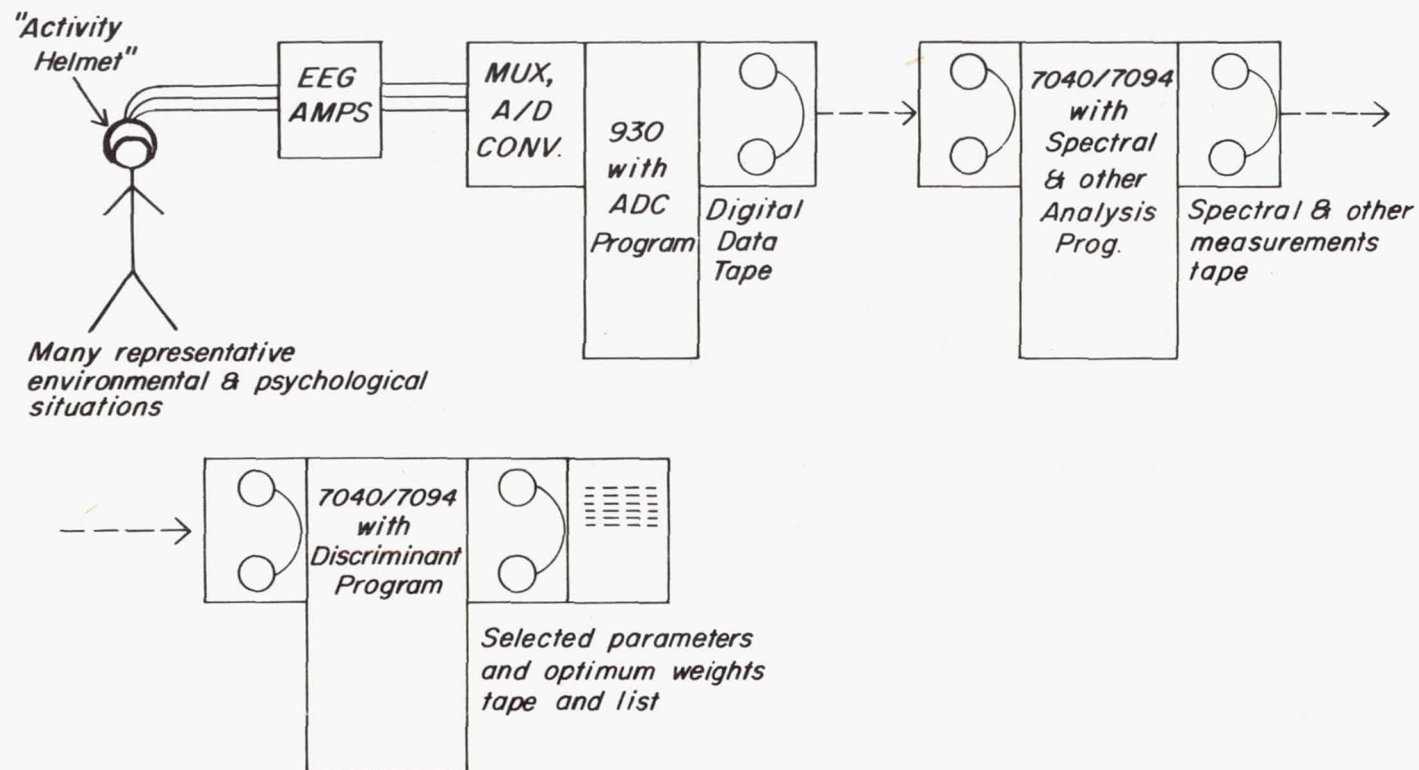
Figure 7. - Analysis of baseline and Gemini GT-7 flight EEG data.

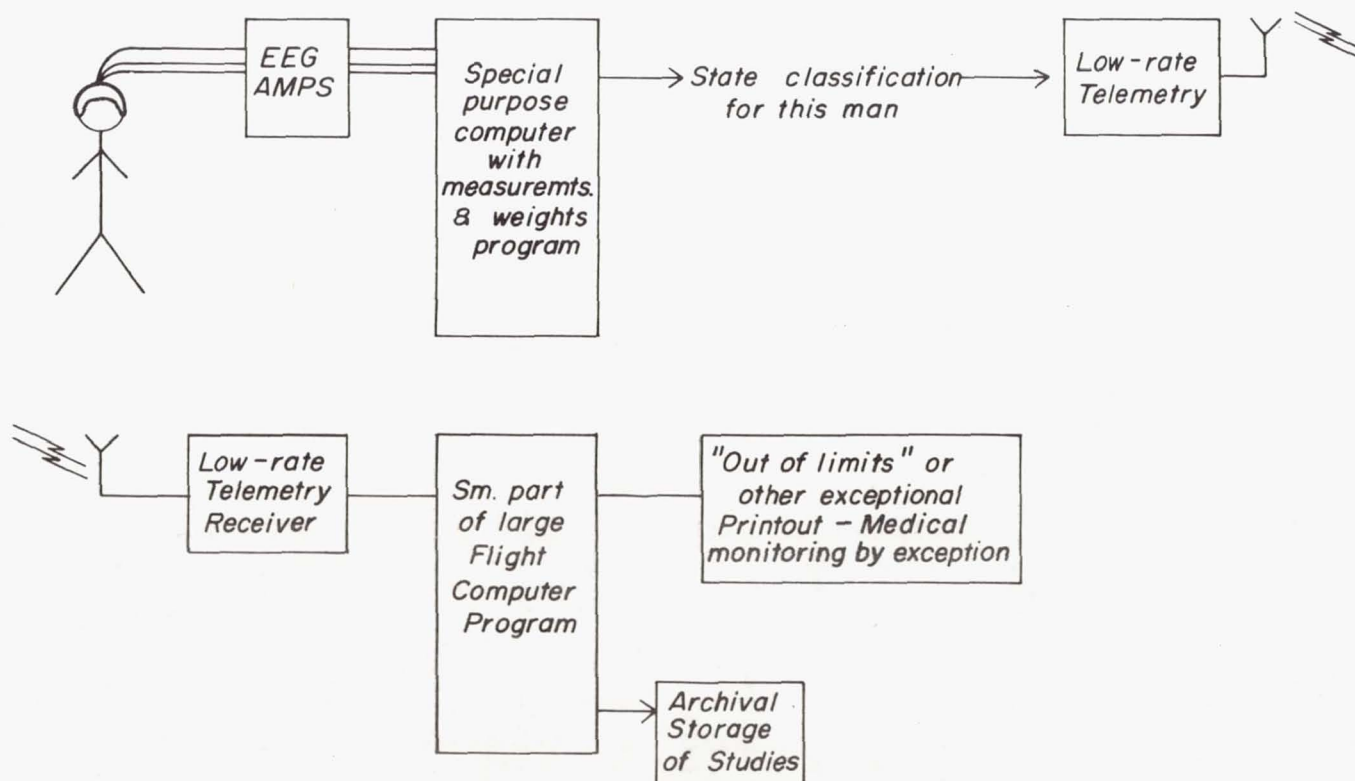# COMPUTER-ASSISTED ASTRONAUT MONITORING METHOD

II. Application Phase

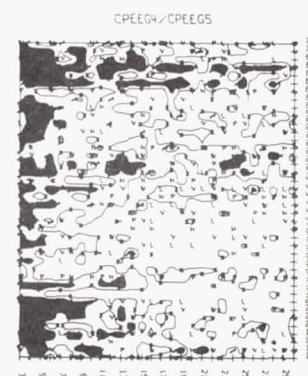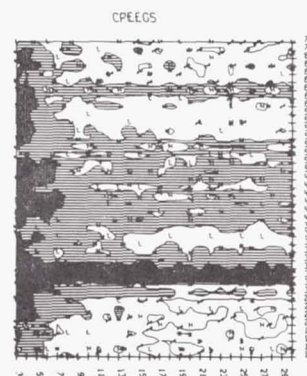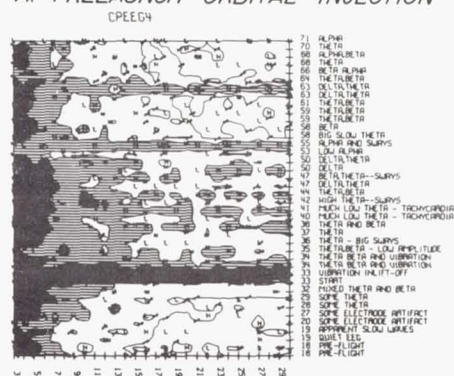Figure 8. - Analysis of baseline and Gemini GT-7 flight EEG data.

To afford a fine-grained analysis (see fig. 9), the prelaunch
period and a substantial part of the first orbit were analyzed on the
basis of two consecutive 10-second samples from approximately every
minute. The prelaunch period was characterized by increased amounts
of theta rhythms (4 to 7 cycles per second) than occur normally in the
resting state. These theta rhythms may be interpreted as relating to
strongly focused attention and orienting responses in a novel situation.
At one minute before lift-off, there was an increment in this activity
and in the higher frequencies in the alpha and beta bands. The power
density of the EEG was augmented by a factor of ten over many frequen-
cies in the period immediately preceding and following launch, which
indicates a strong "arousal reaction" in the classic neurophysiological
sense. Thereafter, there was a slow decline in these augmented den-
sities, with recurrent epochs of higher powers in the higher frequency
bands above 10 cycles per second in the first half hour of flight.
Epochs with gross movement artifacts have been deleted from these com-
puted analyses, and in general, the records are remarkably clean. A
low frequency cut-off of three cycles per second was arbitrarily des-
ignated in the computation to minimize contamination of the analysis
by movement artifacts.

There was only a slow decline in the amount of theta activity in
the early hours of flight and the findings indicated persistence of
substantial amounts of theta activity in the major part of the waking
records throughout the 54 hours of available data. A baseline data
tape for Astronaut Borman, collected according to the techniques of the
normative library by Kellaway and Maulsby, has recently been made
available to us and will be examined. Meanwhile, visual inspection of
the baseline data suggests that there is augmented theta activity in
the flight record in the awake state by comparison with the baseline.

With the prime interest in this experiment centered on drowsiness
and sleep, analyses of subsequent data were displayed, which emphasized
these phases. During the waking state, two consecutive 15-second
samples were analyzed every 10 minutes. During the drowsy and sleep
states, two consecutive 10-second samples were taken every 2 minutes.
The graphic display emphasizes even brief drowsy episodes.

From the third to the seventh hour of flight (see fig. 10), the
subject was awake with occasional drowsy episodes, which the EEG and
computed analyses reveal in the absence of concomitant changes in res-
piration or heart rate. Often these epochs lasted from 3 to 15 seconds
but were manifested in the EEG records.
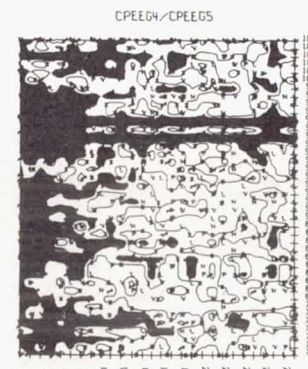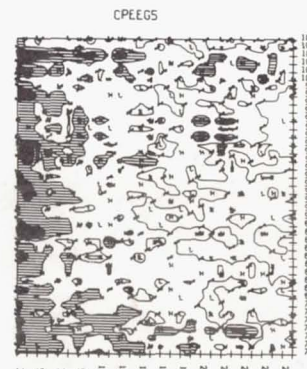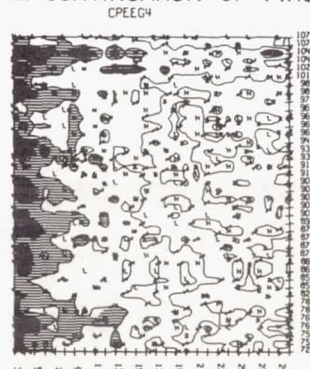
Figure 9. - Analysis of baseline and Gemini GT-7 flight EEG data.

GEMINI GT-7
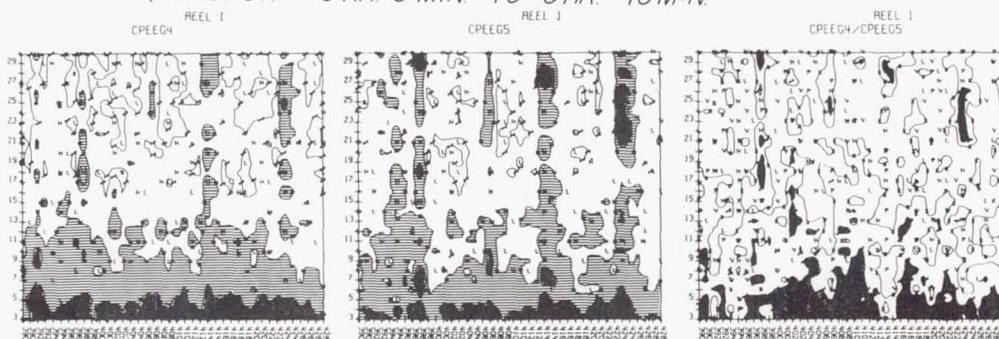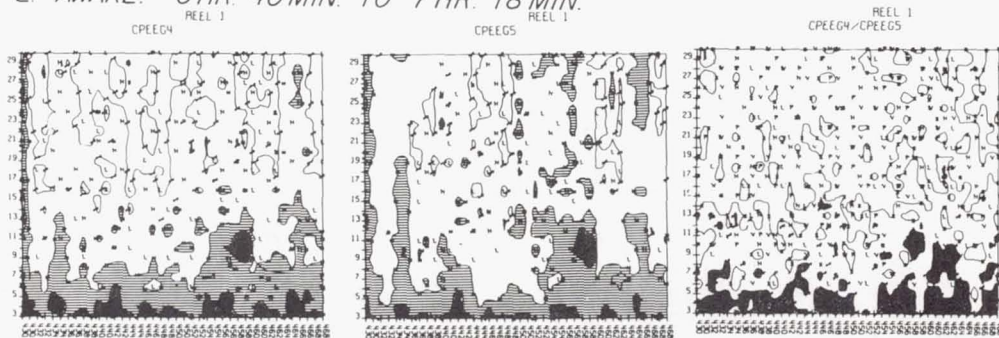
C. ALERT, BECOMING DROWSY. 3 HR. 20 MIN. TO 5 HR. 58 MIN.
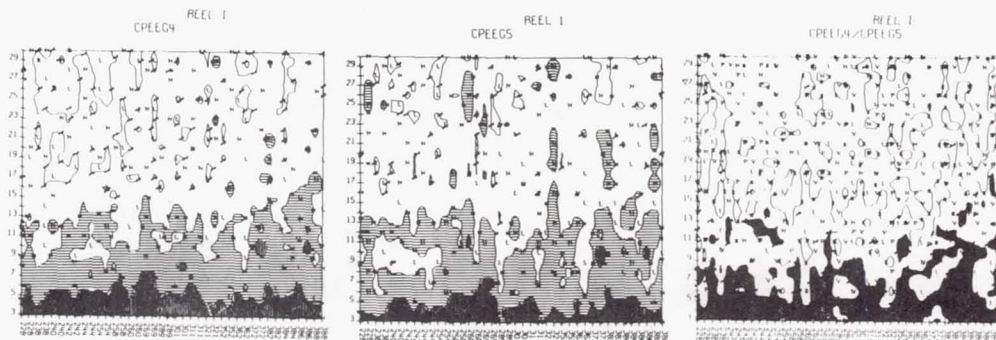
D. AWAKE, DROWSY. 6 HR. 0 MIN. TO 6 HR. 40 MIN.

E. AWAKE. 6 HR. 40 MIN. TO 7 HR. 18 MIN.

Figure 10. - Analysis of baseline and Gemini GT-7 flight EEG data.

From the 15th to the 21st hour, there were long episodes of drowsiness and light sleep, with a brief episode of slow-wave sleep in the 16th hour (see fig. 11). By contrast with the waking states, coherence (right-hand figures in each row) between the two channels rose sharply with onset of drowsiness and actual sleep, corresponding to the increasing synchrony observed on the paper records. A period of wakefulness occurred at the beginning of the 18th hour, characterized by much theta activity, and was followed by drowsiness and light sleep in the 21st hour.

From the 21st to the 23rd hour there was a gradual progression toward full wakefulness and decreasing drowsy episodes (see fig. 12). Compression of almost 5 hours of wakefulness into a single display is shown in the middle panel of figure 12 and shows only occasional drowsy episodes. Coherences remained low through this period, however, except during the drowsy episodes. More frequent drowsy episodes occurred during the 29th hour.

There was a long epoch of medium and deep sleep during the second "night" in space, which was characterized by long periods of uninterrupted slow waves. Even here, however, computer analysis shows the transitions in states over many hours (see fig. 13). At this stage, only one channel remained operative because of an inadvertent detachment of electrodes by the astronaut and only autospectra for this channel could be calculated. It is apparent that even a single channel of data appropriately analyzed can reveal the changing states. Moreover, the EEG reveals changes in pattern during shifting states of sleep and wakefulness not detectable with EKG or respiration (see fig. 14).

Certain significant questions remain unanswered by this study. First, on the basis of further analysis of baseline data, it should be possible to answer categorically the question of apparent preponderance of theta rhythms in the waking state in the flight records. If this should prove to be the case, it would be interesting to seek its persistence over longer periods of flight because it may represent an adapting phenomenon to the strange and, indeed, hazardous environment of space. It is for this reason that lengthy recordings initiated, for example, after the fifth day of prolonged flights would be particularly useful for revealing the extent of adaptation to the space environment. Such additional information would also be relevant to the evolution of sleep patterns during prologned flight. It may be relevant that the data from two nights of sleep does not indicate any paradoxical or REM (rapid eye movement) sleep that is associated with the dream phase and approximately 20 percent of a normal night's sleep. It may be that the location of the electrodes in the anterior lead are too
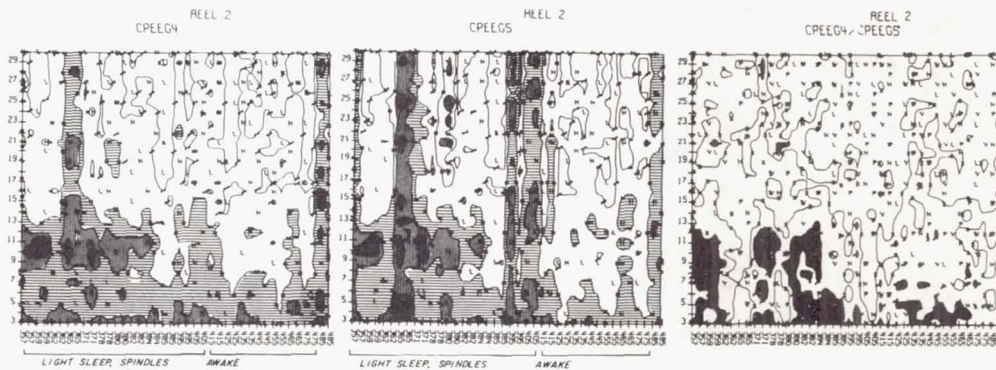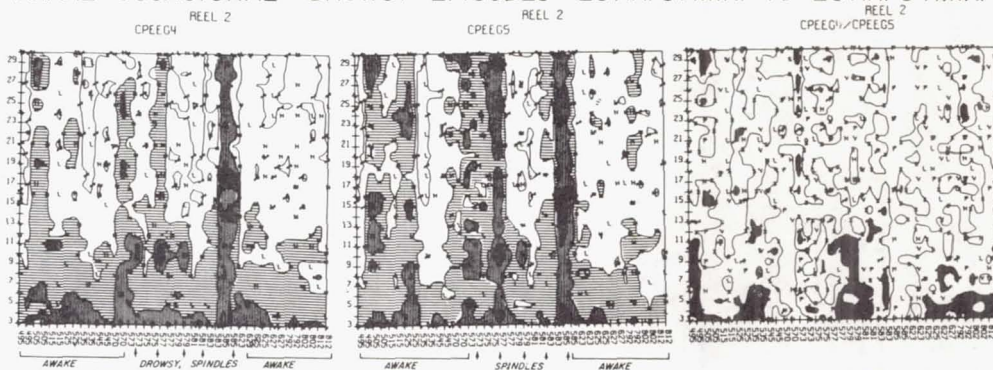
Figure 11. - Analysis of baseline and Gemini GT-7 flight data.
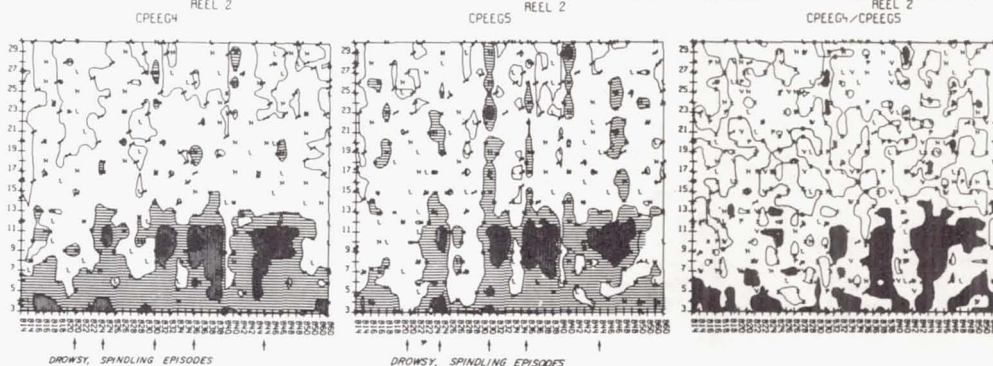
Figure 12. – Analysis of baseline and Gemini GT-7 flight EEG.

GEMINI GT-7
DEEP SLEEP - 35HR. 0MIN. TO 37HR. 36MIN.

REEL 4
CPEEG4

REEL 4
CPEEG4

REEL 4
CPEEG4

REEL 4
CPEEG4

BIG, SLOW WAVES

SPINDLES & SLOW WAVES | AWAKE

AWAKE, SPINDLES | SPINDLES & SLOW WAVES

SLOW WAVES | SPINDLES & SLOW WAVES | SLOW WAVES

MEDIUM & DEEP SLEEP 37 HR. 38MIN. TO 39HR. 50MIN.

REEL 4
CPEEG4

REEL 4
CPEEG4

REEL 4
CPEEG4

SLOW WAVES & OCCASIONAL SPINDLES

MEDIUM SLOW WAVES

SLOW WAVES | SPINDLES & SLOW WAVES

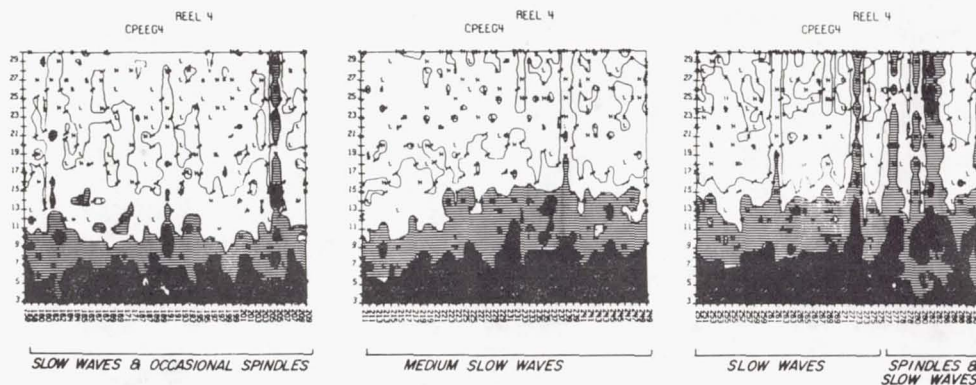Figure 13. - Analysis of baseline and Gemini GT-7 flight EEG data.

EEG IN SPACE FLIGHT - GEMINI GT-7
ASTRONAUTS A and B

A 190 MINUTES AFTER LAUNCH - DOMINANT THETA RHYTHM

RESP A
RESP B
EKG A
EEG1 A
EEG2 A
EKG B
CAPSULE CLOCK

B 420 MINUTES AFTER LAUNCH - DOMINANT ALPHA RHYTHM WITH BRIEF THETA BURSTS

C 506 MINUTES AFTER LAUNCH - DROWSY EPISODE WITH SPINDLES

D 970 MINUTES AFTER LAUNCH - DEEP SLEEP WITH SLOW WAVES   2 SEC
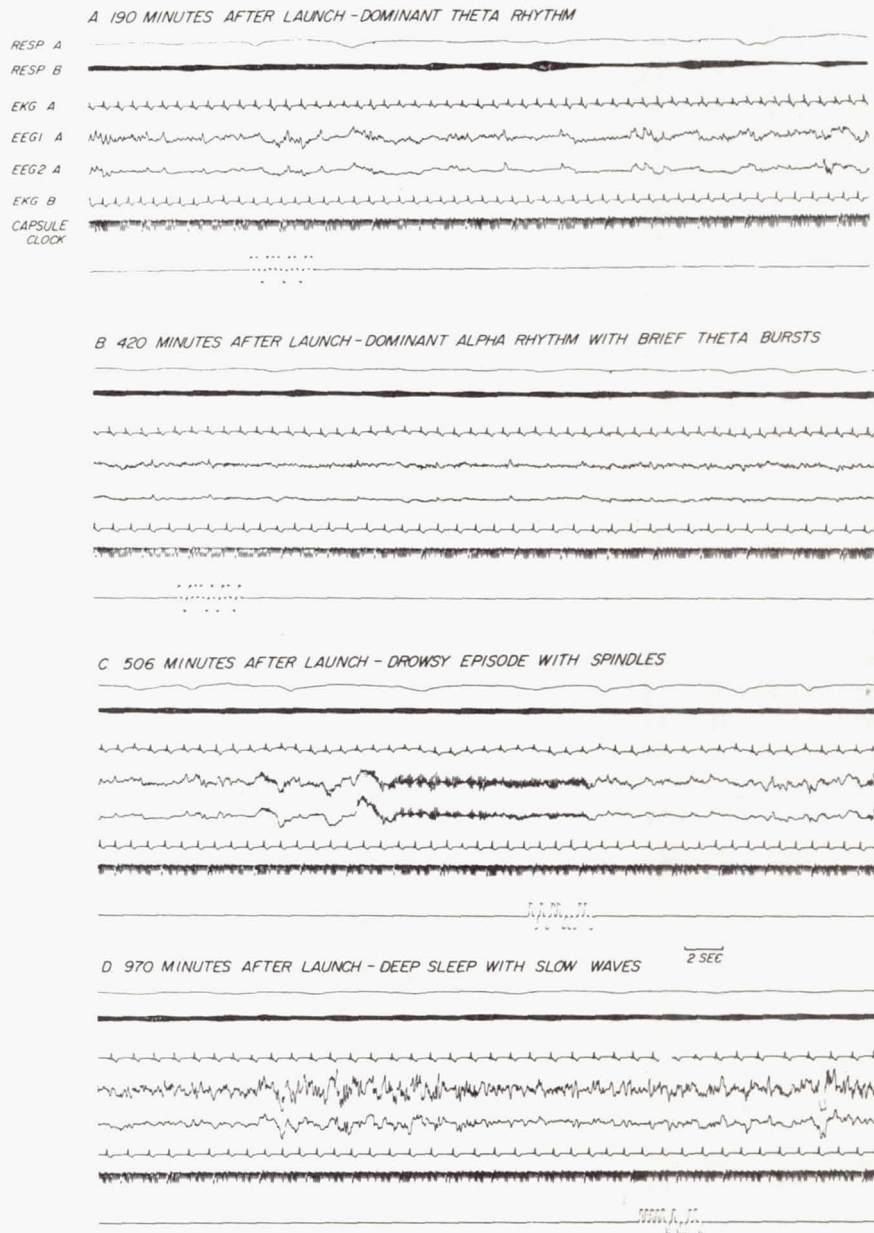
Figure 14. - Analysis of baseline and Gemini GT-7 flight EEG data in specification of on-line computing requirements.

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posterior to record the EOG potentials although blink artifacts are clearly present. In any event, the characteristics of the EEG records from the locations used are not indicative of dream sleep. Clarification of this point would be a simple matter if, in the future, electrodes were placed in inferior frontal positions. From the bioinstrumentation point of view, it would be desirable to consider nonadhesive, zero contact-potential electrodes, inserted into a "bathing cap" for simple wearing or removal by the subject (Kado, Zweizig and Adey, 1965). This would allow initiation of recording at any desired phase of the flight, and eliminate problems of preflight adhesive fixation.

SUMMARY

From analysis of EEG data from a population of 50 astronaut candidates, evidence has been presented, or common characteristics that separate a gamut of conscious and sleeping states, including concomitants of vigilance and decision-making tasks. Extensive digital computing methods for spectral analysis were used, with display techniques that are suited to medical monitoring. Computer recognition of these states by discriminant analysis has indicated the feasibility of on-line computation by special purpose flight computer, using minimal numbers of data channels, and as few as four variables in each channel. The essential requirements are discussed for on-line computation and display. Application of these techniques to EEG data from the flight of Gemini VII are discussed. The analyses emphasize the value of the EEG in detection of both slow and rapid shifts in states of sleep and wakefulness beyond levels that can be detected by observations of EKG and/or respiration.

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AN OBJECTIVE APPROACH TO THE ANALYSIS OF TILT TABLE DATA

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The use of the tilt table to assess man's adaptive ability in changing from the horizontal to the upright position came into use soon after man began to utilize the airplane. The introduction of the tilt table to aviation medicine as a test to express the physical fitness of a pilot, as well as a predictor of his ability to adjust to various body positions while flying, came later, almost as a natural occurrence. Its use then was extended from a test to describe physical fitness to one which would correlate with the ability of man to withstand increased radial accelerative forces. Also, attempts were made to correlate the patient's history of syncope with the tilt table response. Finally, the tilt table has been used in the field of aerospace medicine to provide a provocative test for the evaluation of cardiovascular integrity before and after experiments to simulate weightlessness, as well as before and after manned space flights.

The tilt table test is used to evaluate the integrity of the normal adaptive mechanisms and reflexes which regulate heart rate, blood pressure, vasomotor tone, brain perfusion, and a host of other changes which occur when a person is changed from a horizontal to a vertical position with respect to gravity. The usual response when a normal person is changed from the horizontal to the upright position is characterized by an increase in heart rate, a slight increase in diastolic blood pressure, and a slight decrease in systolic blood pressure. An abnormal response usually is described as a progressive change in blood pressure and heart rate which results ultimately in syncope. Various classifications have been applied to the syndromes or circumstances that result in such responses.

Crampton, in 1914, recognized the potential value in describing the physical condition of a person by evaluating the cardiovascular response to changes in posture. But, he states, "The success of health and vitality increasing measures is difficult to estimate on account of lack of tests. It is highly desirable to obtain some test of the important body function which will show clearly and rapidly by its

variations, the beneficial or depressive effect of various conditions
supposed to affect health." Further, he stated, "Such a test will be
useful in proportion to the importance of the function tested and its
accuracy in recording variation of this function." Some 6 years later,
in discussing the interpretation of the postural changes observed, he
stated, "This mechanism is complex and physiologists are not in accord
to the significance which should be attached to the tone of the
splanchnic veins and various other factors." He was inclined, after
consultation with several of his associates, "to await the dissection
of this phenomenon by the physiologist, and for the present to consider
the discharge of the series of functions which cause blood to return to
the heart in the vertical position as the gravity resisting ability of
the circulation."

In recognizing the potential usefulness of such a test, Crampton
recognized the requirements and limitations imposed upon data inter-
pretation. This is presented clearly by observations he made in the
study of normal persons and patients in his attempt to classify and
correlate postural adjustments with physical condition and health.
Other investigators have shed some light upon many of the operative
mechanisms effecting the postural response in both the normal and disease
states. There still are mechanisms and reflexes, however, which are not
defined accurately, and extension of the use of the tilt table into
aviation medicine has placed even stronger requirements upon the need
for methods to evaluate the responses observed.

The need for a measure to quantify a tilt table response for a
given individual, on a given day, for a given set of environmental or
experimental circumstances, thus became obvious. Evaluation of the
comparative response of the same person from day to day, the comparative
response of a group of individuals, and the comparative response of an
individual before and after various experimental conditions grows more
complicated as the need to detect small changes increases. The inter-
pretation of tilt table data is complicated further by the occurrence
of syncope in a moderate percentage of normal people, although many of
these persons show a medical history that would correlate with the
abnormal tilt table responses. Lack of knowledge of the function and
significance of many physiological and sometimes pathological mechanisms
which result in an abnormal tilt table response makes it difficult to
score or evaluate the significance of many tilt procedures, especially
as one attempts to detect and interpret small changes in an individual's
tilt response that would represent a difference for that individual
while still being within the range of normal response determined for a
group of individuals.

Since the description of the scoring criteria of Crampton, one of the first attempts to provide an improved, comprehensive, statistical approach to the interpretation of tilt table data was described by Graybiel and McFarland in 1941. The utilization of the work of these two men, or the development of improved techniques for tilt table analyses, has been lacking in aerospace medicine. Criteria have varied from specific observations to correlation of several measurements. Some of the many different criteria of measurement of a tilt response used by other investigators are presented from selected papers as follows: the occurrence or non-occurrence of syncope, subjective symptoms of the subject, minimum pulse pressure, time of occurrence of minimum pulse pressure, maximum heart rate, change in heart rate, average changes in heart rate and blood pressure, changes in blood pressure, rates of change of linear curves fit to heart rate and blood pressure data, changes in tissue and venous pressure, blood volume, catecholamine response, electroencephalogram changes, peripheral blood flow, response to the Valsalva maneuver, cardiac output, central venous pressure, peripheral resistance, and leg circumference changes. In many instances, the criteria for evaluation of a tilt have been defined so poorly that some doubt is left concerning the basis for interpretation of data.

It is the purpose of this paper to describe a statistical approach for the evaluation of many of the criteria used by other investigators, as well as for the validation of additional selected measurements. As described, the approach uses only heart rate and blood pressure information as it is acquired typically by most investigators from tilt table procedures. A more comprehensive approach for the evaluation of tilt table data obtained in relation to many other measurements is in progress and will be describe in a later paper.

METHOD

This technique of analysis was directed to the use of heart rate and blood pressure information acquired in tilt table studies conducted at the Texas Institute for Rehabilitation and Research. Baseline data were obtained in a 5-minute control period before tilting the subject to the 70° head-up position, where he remained for 20 minutes unless syncope or impending syncope occurred. Blood pressure information was obtained periodically by the cuff-microphone version of the ausculatory technique, or continuously by arterial puncture. Electrocardiographic data were recorded continuously in all tilt table tests. Data were displayed on strip chart recordings for visual evaluation and analysis, and were recorded on magnetic tape to provide optimum storage and retrieval capability for use by automatic computer techniques. The

computer technique described in this paper was devised to use only a portion of the data collected in order to provide a technique which would be compatible with data collection techniques used by other investigators.

Heart rates used in this analysis represent the total number of QRS complexes in successive minute intervals. Blood pressure measurements were systematically selected by using the value at the beginning of each minute when continuous arterial measurements were taken, or by using the first reading of each minute when cuff-microphone measurements were taken. Combinations or derivations of basic measurements were selected to describe the characteristic heart rate and blood pressure changes occurring during a tilt procedure. They also describe characteristic patterns of change, which may be representative of, or implicate certain reflex or regulatory mechanisms involved in the adaptive response of a subject in transferring from the horizontal to the vertical position.

Discriminant analyses using a step-down regression technique were applied to a variety of measurements to evaluate their relative importance in characterizing the results of tilt procedures; measurements selected by this procedure then were analyzed in more detail. A least squares analysis of variance technique was utilized to describe the statistical significance of measurements made under different circumstances. The following direct measurements or derived values were selected for detailed analyses.

Time to tilt down (minutes).- Time to tilt down expresses the duration from the start of the tilt procedure to the minute after the subject was tilted down; the duration of the control period (consistently 5 minutes) is included in this measurement. As the measurements used in the analysis represent minute values, the time to tilt down expresses the time after the subject was returned to the horizontal position; if syncope occurred at 9.5 minutes after tilt up, time to tilt down then would be expressed by the next minute value plus the 5-minute control period to give a value of 15 minutes. Subjects were tilted down with the occurrence of syncope or when symptoms and observations were such that syncope was imminent. As such, this measurement also is a measure of the occurrence or non-occurrence of syncope, since a standardized time in the head-up position has been established as 20 minutes duration.

Average heart rate pretilt (beats/minute).- This measurement represents the average of the minute heart rates for 5 minutes of baseline data obtained prior to tilting the subject to an upright position. This measurement was selected for its general usefulness as one criteria which frequently distinguishes athletic and nonathletic types of individuals. In addition, it provides an objective measurement to describe baseline

heart rate changes which occur as a result of an experimental procedure: for example, heart rate generally has been described to increase during bedrest and decrease during water immersion. The use of this most important measurement to provide baseline information on an individual assumes that the individual truly is baseline; familiarity with the test laboratory and equipment, as well as the tilt procedure through previous exposure and simulated testing, is necessary to minimize the effect on anxiety of this measurement.

Maximum heart rate during tilt (beats/minute).- This value represents the greatest heart rate during tilt in the upright position, and uses the total minute heart beats as described above. This is a type of average rate to describe the maximum heart rate, and does not represent the maximum heart rate based on conversion of the R-R interval to an instantaneous rate. The measurement was selected to allow use of data from a variety of investigations. Consideration of the instantaneous heart rate, its maximum value, and patterns of change will be discussed in a future paper in which a more detailed analysis is described.

Minimum heart rate after tilt (beats/minute).- Minimum heart rate after tilt represents the lowest of the successive 1-minute total heart beats occurring immediately after tilt down. This measurement was selected for the potential information it might give on the pattern of recovery. For example, a "normal tilt" with a large overshoot in heart rate might indicate the presence of very effective mechnisms in the upright position which would compensate for the pooling of blood. Upon being tilted down, the subject's blood then would become available for immediate return to the heart, with a resultant decrease in the heart rate. Failure to have an overshoot could represent faulty reflex mechanisms after tilt down, inaccessibility for return to the heart of pooled blood or its component plasma, or failure of blood pooling. Distinction between these possible responses would come from evaluation of other data taken during the tilt, such as leg circumference change, venomotor tone, and blood pressure and heart rate changes occurring in the upright position.

Change in heart rate with tilt (beats/minute).- The difference between the maximum minute rate during tilt and the average pretilt rate is represented by change in heart rate with tilt.

Fractional increase in heart rate.- This measurement is the quotient of change in heart rate with tilting and the average heart rate pretilt. The expression gives consideration to the initial or resting value of the change in heart rate during tilting.

Average heart rate pretilt minus average heart rate posttilt
(beats/minute).- The difference between the average of the 1-minute
total heart beats for 5 successive minutes prior to upward tilt and
the average of the 1-minute total heart beats for the 5 minutes immed-
iately after tilt down is another expression of the overshoot that
occurred after tilting the subject back to the horizontal position.

Time of maximum heart rate (minutes).- This measurement defines
the duration the subject was in the head-up position at which time the
1-minute interval heart beats reached its maximum value. To interpret
this measurement, one must consider its relationship to the maximum
heart rate and the pattern of change in heart rate. For example, a
short time to reach maximum heart rate could be an indication of a
large amount of venous pooling, with an immediate increase in heart
rate. An initial large change in heart rate, with a further progres-
sive increase in heart rate resulting in a lengthened time to maximum
heart rate, could represent occurrence of further pooling, extravasa-
tion of fluid into the extravascular space, or deterioration of other
compensatory mechanisms. As used in this analytic technique, this
measurement was selected as a means to test for any characteristic
change by application of a sound statistical approach. Interpretation
of statistical changes then would require consideration of other
measures or related observations which might help to differentiate
the possible conditions.

Time to 80 percent maximum heart rate (minutes).- This value
represents the time after tilt to the upright position at which the
total minute heart beats reached a value greater than 80 percent of
the total change in heart rate during the tilt procedure. It was
selected as probably representing the heart rate change associated
most directly with the venous pooling of blood, and thus would be
one reflection of the decreased availability of blood for return to
the heart, the decrease in cardiac output, and the effect of carotid
sinus stimulation resulting from blood pressure changes. A more
refined distinction between the immediate change in heart rate and
the slower progressive change in heart rate is presented below by
considering the intercept of two lines statistically fit to heart
rate data obtained during the time the subject is in the upright po-
sition.

Time to plateau of heart rate (minutes).- The heart rate is de-
fined as reaching a plateau when a successive minute total heart rate
has not increased over the preceding minute total, after the subject
has been upright for 1 minute. This expression was selected as a
potential means of indicating the time of occurrence of additional
compensatory mechanisms which might be called into operation to pro-
tect against progression of changes frequently observed with a tilt.

Slope to 80 percent heart rate (beats/minute/minute).- This is a reflection of the magnitude of change in heart rate as well as the rapidity with which it occurred. It represents the quotient of the change in heart rate at the time defined above, and the time elapsed during which the subject was in the upright position.

Slope to plateau (beats/minute/minute).- This slope reflects the change in heart rate at the time of occurrence of the plateau divided by the duration of tilt in the upright position.

Average pulse pressure pretilt (mm Hg).- This measurement represents the average of the pulse pressures obtained during the 5-minute baseline period prior to tilting the subject to the upright position. Pulse pressure is defined as systolic minus diastolic pressure.

Minimum pulse pressure during tilt (mm Hg).- This is the lowest successive minute pulse pressure obtained during the tilt. Considerably different ranges of values for this measurement will be found depending upon the technique of obtaining blood pressure. When the subject is in the upright position, blood pressure obtained by the ausculatory technique yields much narrower pulse pressures than direct arterial pressures; the reason for this primarily is because of difficulty in discriminating the reading of the diastolic measurement by the indirect technique.

Average pulse pressure pretilt minus minimum pulse pressure during tilt (mm Hg).- This measurement expresses the absolute change in pulse pressure during tilt.

Fractional decrease in pulse pressure.- The ratio of the change in pulse pressure to the average pulse pressure prior to upward tilt is classified as fractional decrease in pulse pressure.

Time of minimum pulse pressure (minutes).- This is a measure of the time from tilting the subject to the upright position to the time of occurrence of minimum pulse pressure. Interpretation of significant changes in this value must consider the pattern of change. For example, a shortened time to occurrence of the minimum pulse pressure could represent stabilization of pressure in a normal tilt response; or, it could represent the greatly shortened time to the occurrence of minimum pulse pressure in a tilt procedure on a deconditioned subject caused by a drop of blood pressure and resulting syncope.

Slope of diastolic blood pressure (mm Hg/minute).- This measurement expresses the slope of the line representing the best linear curve fit of successive minute diastolic blood pressure measurements taken beginning 1 minute after tilt up. The relationship to slope of other

pressure and heart rate measurements gives some indication of the cardiac output and peripheral resistance changes which may occur during tilting. The slope may be positive or negative depending upon the condition of the subject, and the duration of the tilt.

Slope of systolic blood pressure (mm Hg/minute).- Slope of systolic blood pressure is the slope of the line representing the best linear curve fit to successive minute systolic blood pressure measurements taken beginning 1 minute after tilt up. This slope is usually more negative than is found for diastolic blood pressure.

Slope of mean blood pressure (mm Hg/minute).- This value represents the slope of the line representing the best linear curve fit to mean blood pressure measurements, where mean blood pressure is defined as the sum of diastolic pressure and one-third of systolic minus diastolic pressure, that is, $\left[D + 1/3(S - D)\right]$.

Slope of pulse pressure (mm Hg/minute).- The determination of slope of pulse pressure provides a measure of the slope of the line representing the best linear curve fit to successive minute pulse pressures. It reflects the change in pulse pressure and the rapidity with which it occurs.

Linear curve fitting has been selected to provide a simple expression of trends of change in heart rate and blood pressure measurements which otherwise would be hard to describe. In many cases, this simple approach is justifiable and has meaning when the tightness of curve fit also is given. Higher order curves, such as polynomials, are easy to estimate, but the many individual coefficients are difficult to interpret. Exponential curves are more useful, but are probably not justified in the approach being described when only periodic samples, such as 1-minute average measures, are used. Further refinement in the simplified linear curve fitting approach is described below by considering the best fit of two lines to the data collected in the upright position. Such an approach was selected as a potential means to represent changes which might give clues to indicators of different mechanisms of compensation or decompensation that occur during a tilt test. This two-line approach enables a clearer definition of the break between two possible mechanisms.

Time at break in two heart rate curve fits (minutes).- This measurement represents the time of the minute reading immediately preceding the occurrence of the intersection of two best fit linear curves to the heart rate pattern observed in response to tilt to the upright position. It is measured from the start of the tilt to the upright position; therefore, it does not include the 5-minute baseline period prior to the

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time of placing the subject in the head-up position. This measurement
was selected for the potential information it might contain on indicat-
ing the time of progression from one physiological control mechanism
to another.

   Heart rate at break (beats/minute).- Heart rate at break represents
the sum of the minute heart beats for the minute preceding the time of
occurrence of the intersection of the two lines fit best to heart rate
data obtained during the head-up position.

   Slope of the first heart rate data line (beats/minute/minute).-
This value is the slope of the line fit best to heart rate in the
first portion of the head-up tilt procedure. It was selected to repre-
sent the initial changes that occur with tilting and probably is a
reflection primarily of venous pooling and the changes that result
therefrom.

   Slope of second line fit of heart rate data (beats/minute/minute).-
The slope of second line fit heart rate data represents the slope of
the line representing the best linear fit to the terminal portion of
the heart rate data obtained during the head-up portion of a tilt test.
It was selected to be representative of progressive changes (for ex-
ample, transudation of fluids, extension of pooling, et cetera) or to
indicate occurrence of compensatory mechanisms to protect against
further changes during a tilt.

   Standard deviation of residual of best fit heart rate lines
(beats/minute).- This measurement describes the tightness of fit of a
combined best fit of the two heart rate regression lines. It also was
selected as a simplified indicator of the oscillatory and random pat-
terns of change that occur in heart rate during the tilt.

   Time at break of pulse pressure (minutes).- Time at break of
pulse pressure indicates the time immediately preceding the intersec-
tion of two linear regression curves fit best to pulse pressure data
obtained during the upright tilt position. It is measured from the
start of tilt to the upright position.

   Pressure at break (mm Hg).- Pressure at break represents the actual
minute reading of pulse pressure immediately preceding the time of the
calculated intersection of the two best fit lines for pulse pressure
data.

   Slope of the first line fit of pulse pressure data (mm Hg/minute).-
This value represents the slope of the line fit best to pulse pressure
measurements in the first portion of the head-up position.

   Slope of the second line fit of pulse pressure data (mm Hg/minute).-
The slope of the line fit best to pulse pressure data in the final
portion of the head-up tilt is indicated in this measurement.

   Standard deviation of residual of best fit pulse pressure lines
(mm Hg).- This measurement describes the tighness of fit to the pulse
pressure data obtained in the head-up position of a combined best fit
of the two regression lines described above.

                               RESULTS

   A sample analog tracing of the electrocardiogram, impedance
pneumogram, cuff-microphone blood pressure, and time code identifica-
tion are shown on figure 1, indicating the type of data collected
during a tilt. From this record, the successive 1-minute total heart
beats and the one-per-minute sampled blood pressure were tabulated and
entered on punch cards for storage and computer processing. Other
identification data were entered into the punch cards at this time.
The computer programmers, following detailed problem definition sheets,
processed the data to obtain desired plots, tabulation of data, and
statistical analyses.

   A plot of the heart rate and blood pressure data which were pro-
cessed by an IBM 7094 computer, and plotted using an S.C. 4020 plotter
is shown on figures 2 and 3. A plot of systolic, diastolic, mean blood
pressure, and heart rate for a normal subject prior to bedrest is dis-
played on figure 2. The same heart rate and corresponding pulse pres-
sure data plotted to the same time scale are shown on figure 3. The
data plotted for this subject on figures 1 and 2, as printed by the
computer at the time of analysis, are presented in table I. The values
of some of the derived measures which characterize this particular tilt
are shown in table II.

   Figure 4 is a plot of tilt table data for this same subject after
10 days of deconditioning, showing some of the gross characteristics
of deconditioning. Figure 5 is the plot of data on another subject
after bedrest deconditioning for comparison with figures 2 and 4.
Taken as a single tilt table response, it would be hard to characterize
this particular plot as either a normal or abnormal tilt response.
There was a moderate increase in heart rate, with a slight rise in
diastolic blood pressure, and a drop in systolic pressure. This re-
sponse seemed "normal" for the first 5 or 6 minutes after tilt to the
upright position, after which there was an increase in the heart rate
and a stabilization of blood pressure; finally, there resulted a pre-
cipitous drop in blood pressure and heart rate characteristic of vaso-
vagal syncope.

ELECTROCARDIOGRAM

IMPEDANCE PNEUMOGRAM

CALIBRATION

124

124

120

100 mm. Hg.

50

50

54

0

CUFF-MICROPHONE BLOOD PRESSURE
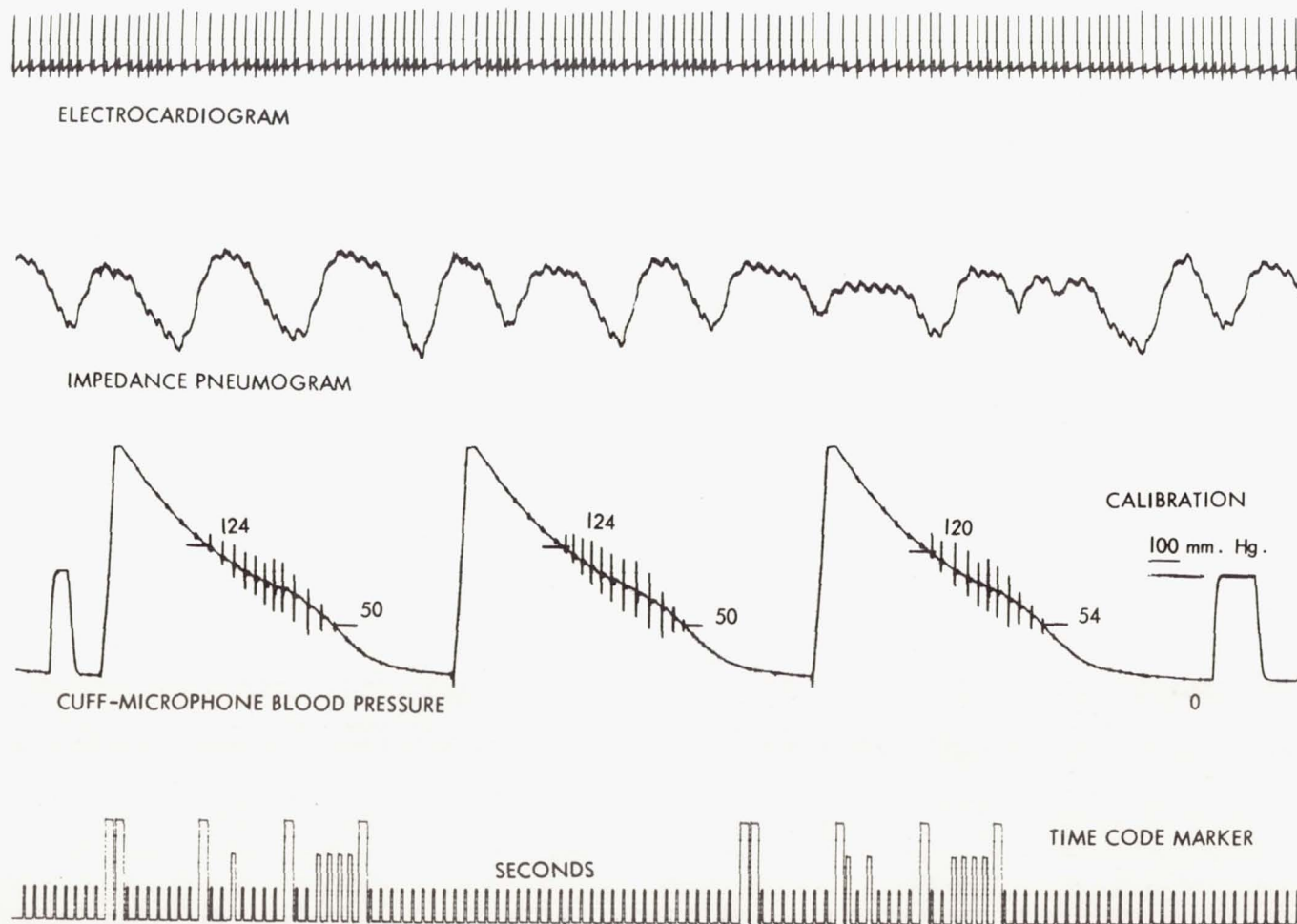
TIME CODE MARKER

SECONDS

Figure 1. - Sample tracing of measurements obtained during tilt.

TABLE I

Tabular Display of Tilt Table Data
Presented Graphically in Figures 1 and 2

W. McArthur   Tilt No. 1 (Complex)
Subject No. 7   July 24, 1964

Tilt up at 6.0 minutes, no syncope, tilt down at 26.0 minutes

Time (min.)	HR (beats/min.)	Syst. BP (mm.Hg.)	Diast. BP (mm.Hg.)	PP (mm.Hg.)	Mean Pressure (mm.Hg.)
1	62	140	72	68	94.7
2	64	146	78	68	100.7
3	65	145	77	68	99.7
4	63	127	75	52	92.3
5	70	140	70	70	93.3
6	80	135	73	62	93.7
7	78	138	75	63	96.0
8	77	135	75	60	95.0
9	76	137	77	60	97.0
10	76	142	60	82	87.3
11	77	126	75	51	92.0
12	77	137	79	58	98.3
13	80	131	78	53	95.7
14	77	141	80	61	100.3
15	77	141	73	68	95.7
16	79	137	80	57	99.0
17	82	133	79	54	97.0
18	81	130	77	53	94.7
19	81	126	76	50	92.7
20	82	135	80	55	98.3
21	83	151	85	66	107.0
22	82	130	78	52	95.3
23	80	130	73	57	92.0
24	81	132	75	57	94.0
25	83	145	78	69	100.3
26	75	138	71	69	93.3
27	60	138	78	60	98.0
28	58	139	74	65	95.7
29	57	140	73	67	95.3
30	59	137	76	61	96.3

TABLE II

Blood Pressure and Heart Rate Measurements With Derived Values
That Characterize the Tilt Table Changes Shown in Figure 1

W. McArthur   Tilt No. 1 (Complex)
Subject No. 7   July 24, 1964

Tilt up at 6.0 minutes; no syncope; tilt down at 26.0 minutes

Average Heart Rate Pre Tilt	64.8	beats/min.
Maximum Heart Rate During Tilt	83	beats/min.
Minimum Heart Rate After Tilt	57	beats/min.
Change in Heart Rate with Tilt	18.2	beats/min.
Fractional Increase in Heart Rate	0.28	beats/min.
Average Pre Tilt HR – Avg. Post Tilt Rate	6.3	beats/min.
Time of Max. HR from start of Tilt Up	15	minutes
Time to 80% Maximum Heart Rate	0	minutes
Time to Plateau	2	minutes
Slope to 80% Heart Rate	15.2	heart rate/min.
Slope to Plateau	4.1	heart rate/min.
Average Pulse Pressure Pre Tilt	65.2	mm.Hg.
Minimum Pulse Pressure During Tilt	50	mm.Hg.
Average Pre Tilt PP – Min. During Tilt	15.2	mm.Hg.
Fractional Decrease in Pulse Pressure	0.23	
Time of Min. PP from start of Tilt Up	13	minutes
Average Pre Tilt Mean Press. – Min. Dur.	8.8	mm.Hg.

	Diastolic	Systolic	Mean BP	Pulse Pressure
Slope	0.2719	-0.0175	0.1754	-0.2895
SSR	392.5877	756.2456	287.8597	1016.7631
SDR	4.8056	6.6697	4.1150	7.7337

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Figure 2. - Blood pressure and heart rate response of a normal healthy person to a tilt table procedure.

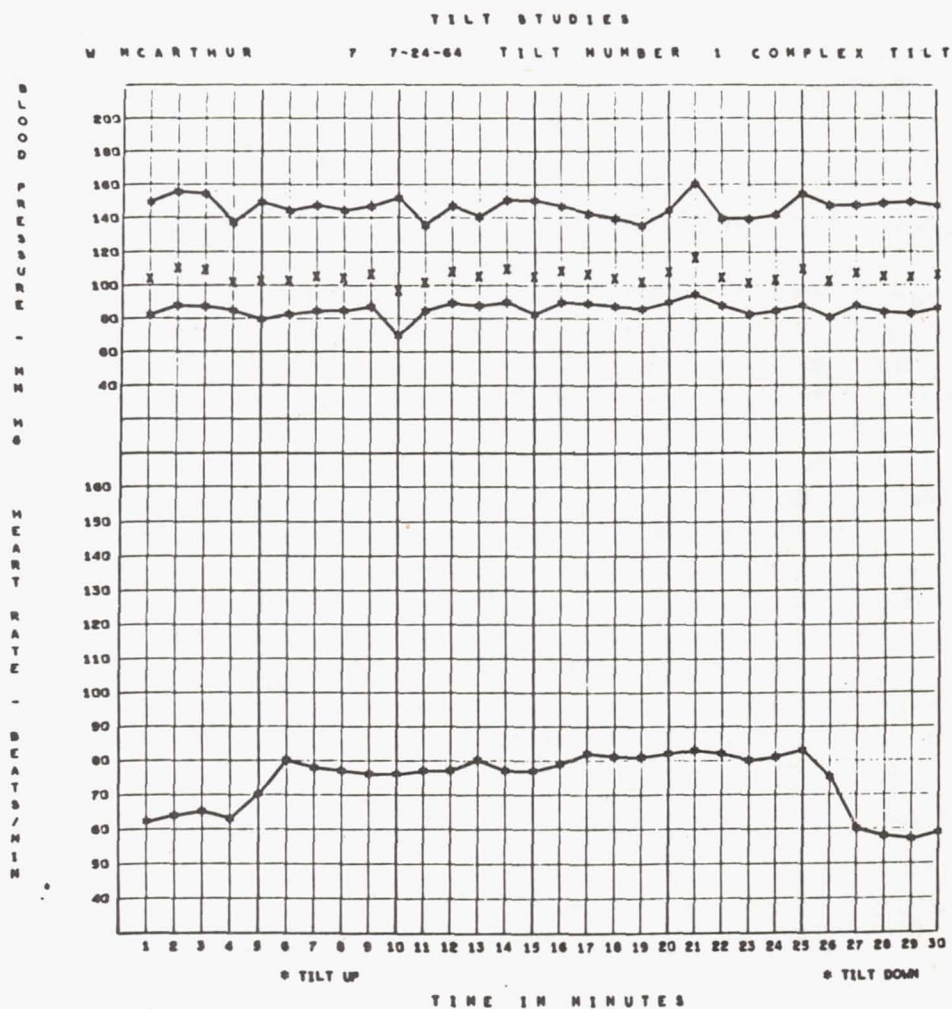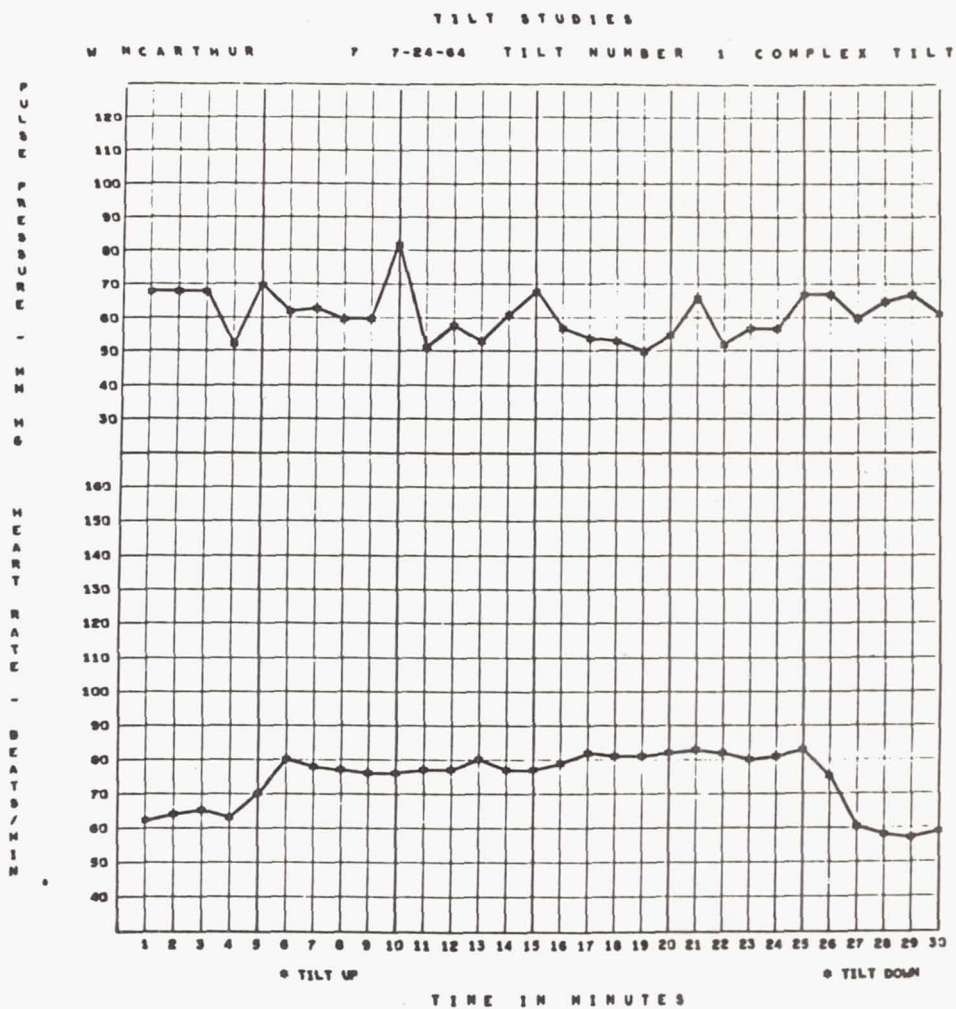The image shows a scientific figure/chart. Page number 393 at top.

Figure 3. - Pulse pressure and heart rate response of a normal, healthy person to a tilt table procedure.
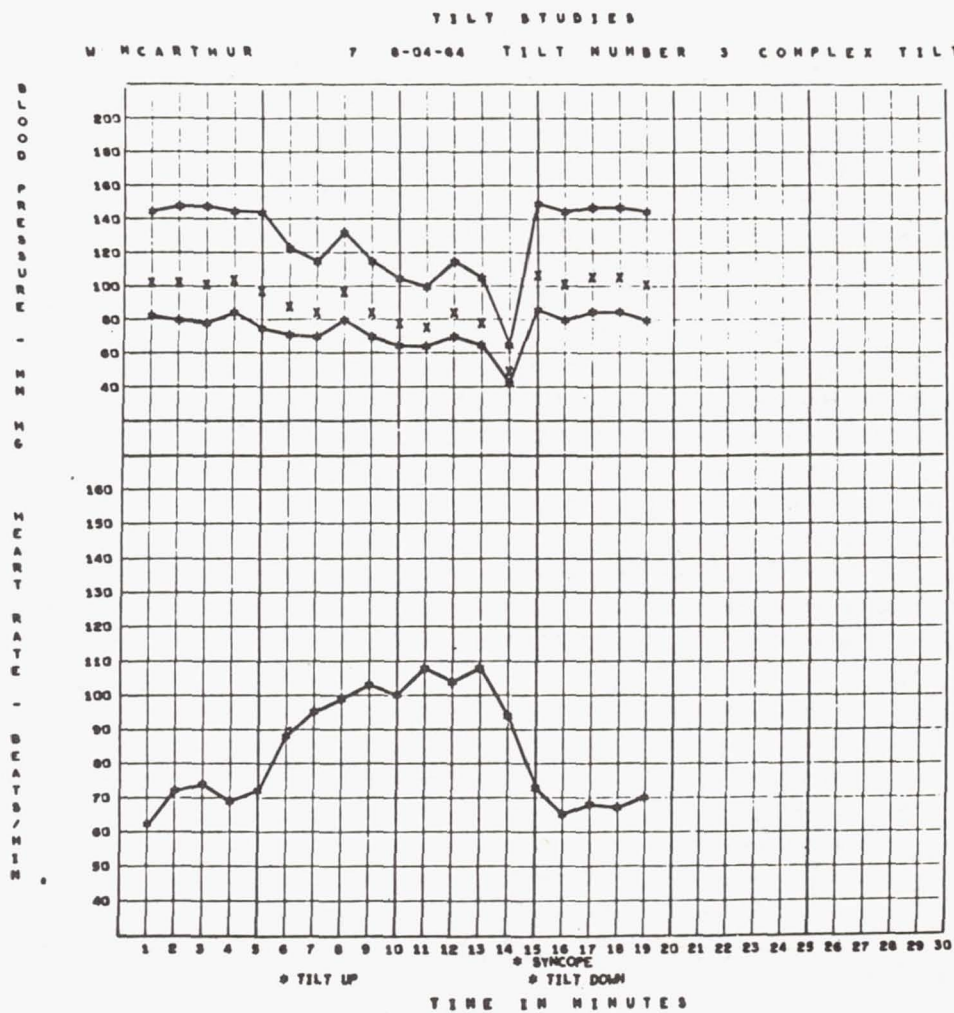
Figure 4. - Blood pressure and heart rate changes in the subject shown in figure 2 after 10 days of deconditioning.
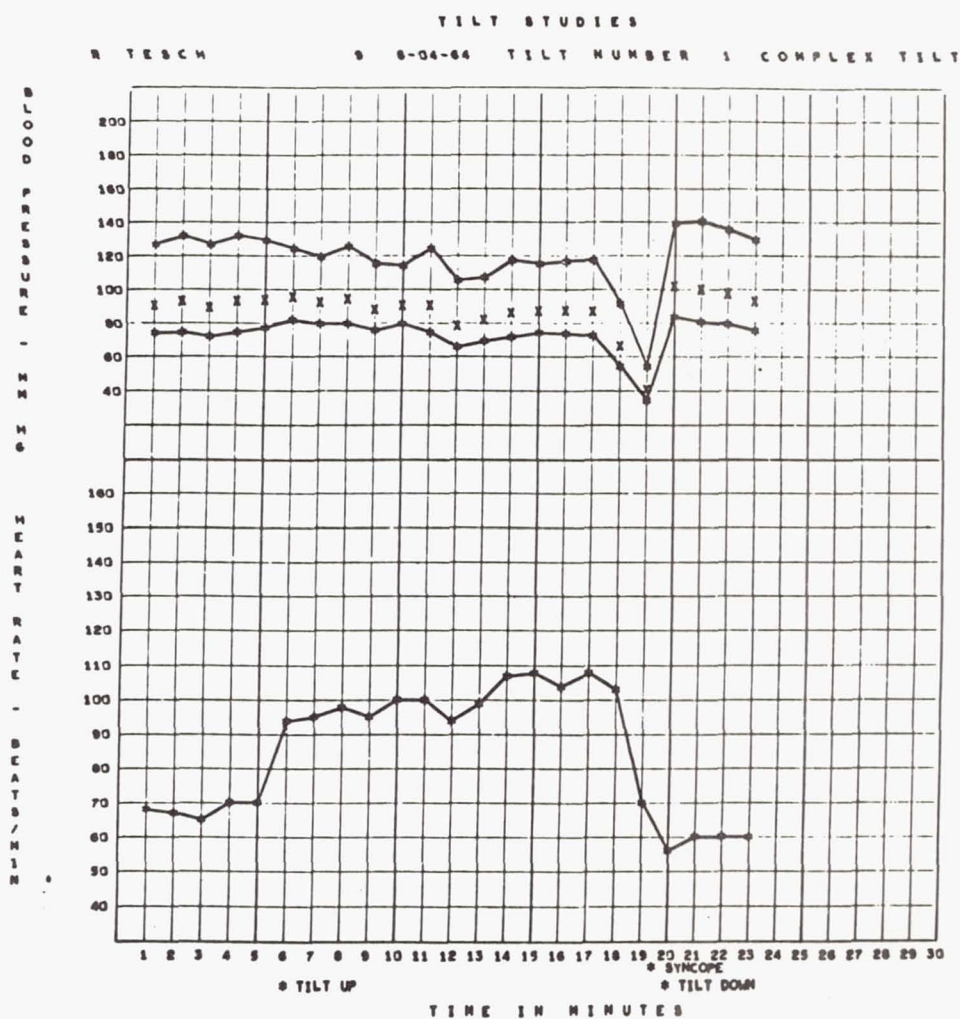
Figure 5. - Blood pressure and heart rate changes in a healthy subject
after 10 days of deconditioning.

In table III is presented the summary of results of an analysis of variance performed on the measurements from the postdeconditioning tilts of a group of 11 subjects who underwent three periods of deconditioning with treatment measures randomly assigned. One subject participated in only one deconditioning experiment and was replaced by a second subject who underwent two periods of deconditioning. As indicated here, the comparative tilt response postdeconditioning showed no difference after the three deconditioning periods. However, there was a difference in response when the nonathlete or athlete category of the subjects was considered as the main effect.

In table IV is shown an analysis of variance for the single measure post-bedrest average heart rate pretilt. The sums of squares were adjusted statistically when the data were not balanced; the means at the bottom of the table were actual means and usually are not very different from the adjusted estimates. There was no significant difference between the heart rates as shown in the table of means for the values at the end of periods 1, 2, and 3 (66.72, 65.86, and 64.94 beats per minute). The comparison of nonathlete and athlete shows a distinct difference in heart rate, with values of 69.48 and 61.67 beats per minute, respectively. The sample size for the nonathlete/athlete comparison shows an imbalance (16-14) for 10 subjects for three periods. This imbalance resulted from replacement of a nonathletic subject after deconditioning period number 1 with an athletic subject. This analysis demonstrates the flexibility of the least squares analysis of variance techniques in manipulating unbalanced data of the type which might be acquired in association with complicated experimental designs where a group of subjects undergo several successive periods of deconditioning for the purpose of serving as their own controls for several experimental conditions.

In table V there is presented another analysis of variance in which the postdeconditioning resting heart rate of the same group of subjects was compared with the predeconditioning resting heart rate. Consideration was given to evaluating the effect of treatment measures randomly assigned during the deconditioning periods. Pooled heart rates for all predeconditioning tilts were compared to postdeconditioning heart rates for the three potential treatments. There was a slight but statistically nonsignificant increase in heart rate after deconditioning. Again there is a highly significant difference in the nonathlete/athlete comparison of resting heart rate. For this analysis comparing athlete and nonathlete groups, both the pre and posttreatment resting heart rates were used. Previous analysis had been performed on the predeconditioning tilts in which there was no significant difference in the tilts; therefore, the predeconditioning tilts were pooled.

TABLE III

Summary of F Values for Measurements and Derived Values
Comparing Response of the Same Group of Subjects
After Three Periods of Deconditioning

	Periods Post-Deconditioning	Non-Athlete Athlete
Time to Tilt Down	0.79NS	2.40NS
Avg. HR Pre-Tilt	0.03NS	4.67*
Max. HR During Tilt	0.52NS	3.89NS
Min. HR After Tilt	0.33NS	7.48*
Change in HR With Tilt	1.07NS	0.13NS
Frac. Incr. in HR	0.76NS	0.94NS
Avg. Pre HR – Avg. Post	0.96NS	2.16NS
Time of Max. HR	0.89NS	2.65NS
Time to 0.8 Max. HR	0.65NS	1.95NS
Time to Plateau	0.75NS	0.53NS
Slope to 0.8 HR	0.30NS	0.88NS
Slope to Plateau	1.33NS	1.38NS
Avg. PP Pre-Tilt	0.33NS	0.78NS
Min. PP During Tilt	1.67NS	4.31*
Avg. Pre-PP – Min. During	0.59NS	1.09NS
Frac. Decr. in PP	0.90NS	3.04NS
Time of Min. PP	3.25 NS	0.35NS
Avg. Pre-Mean – Min. During	0.77NS	7.72**
Slope of Diastolic	1.39NS	0.15NS
Slope of Systolic	0.60NS	0.58NS
Slope of Mean Pressure	0.95NS	0.31NS
Slope of Pulse Pressure	0.99NS	1.27NS

NS = Non-significant
* $p < 0.05$
** $p < 0.01$

TABLE IV

Analysis of Variance of Average Pre-Tilt Heart Rate
On The Same Group of Subjects After
Three Periods of Deconditioning

	dF	SS	MS	F
Total	29.	0.295043945E 04		
Period-Post-BR	2.	0.618182126E 01	0.309091065E 01	0.0323NS
Non-athlete/athlete	1.	0.446479743E 03	0.446479743E 03	4.6656*
Residual	26.	0.248811909E 04	0.956968898E 02	

Table of Means for Main Effects

Period-Post-BR	66.7200	65.8600	64.9400
Sample Size	10	10	10
Non-athlete/athlete	69.4875	61.6714	
Sample Size	16	14	

 * p < 0.05
** p < 0.01

TABLE V

Analysis of Variance Performed to Compare Pooled
Pre-deconditioning, Pre-tilt Heart Rates to
Pre-tilt Heart Rates After Three
Periods of Deconditioning in the
Same Group of Subjects

	dF	SS	MS	F
Total	59.	0.430027926E 04		
Treatment	3.	0.114703133E 03	0.382343780E 02	0.5898NS
Non-athlete/athlete	1.	0.600858894E 03	0.600858894E 03	9.2694**
Residual	55.	0.356518360E 04	0.648215198E 02	
Table of Means for Main Effects				
Treatment	63.4067	65.0000	67.5800	64.9400
Sample Size	30	10	10	10
Non-athlete/athlete	67.6312	61.1857		
Sample Size	32	28		

 * p< 0.05
** p< 0.01

DISCUSSION

An objective, statistical approach has been developed for the analysis of tilt table data utilizing a least squares analysis of variance program on an IBM 7094 computer. The technique provides for graphic, tabular, and statistical displays of data, as well as great flexibility for performing different combinations of statistical analysis with tilt table data.

Such an approach does not provide answers to all questions regarding interpretation of tilt table analyses for different subjects under different experimental circumstances. However, it does provide a means to process large volumes of data and describe significant patterns of change which then may be related to known or postulated mechanisms that result in deconditioning. It also provides a means to relate these changes to known compensatory response patterns which operate under normal and abnormal conditions. For the technique to be used effectively, however, strong consideration must be directed to proper experimental design, proper collection of data (including exposure of a subject to several tilts before acquiring baseline data), and proper choice of the statistical approach and interactions to be considered.

The techniques described represent a simplified version of an approach which is being developed to process data collected continuously during tilt table procedures. Included will be a consideration of the relationships of a tilt procedure to other measurements such as plasma volume, leg circumference changes during tilt, et cetera. It is hoped that this approach ultimately will provide an effective method to categorize the types of tilt table and other responses observed after bedrest, water immersion, and space flight in order to define their similarities and differences. After experience is gained with this approach, perhaps more can be said regarding common mechanisms of deconditioning. Then an organized approach may be directed to defining and evaluating potential or preventive measures.

This paper precedes a series of papers which will use this objective approach and modification of the analytic techniques for tilt table data and other data collected from normal healthy adult males during controlled experimental studies. Primary attention will be directed later to the description of the normal variations in response of an individual to tilting at different times of the day; to describe expected variations which may occur in the tilt responses of an individual from day to day; and to describe the comparative response in simple noninstrumented and well-instrumented tilt table procedures. Characteristic tilt table responses will be described as they relate to the physical status of an individual, such as nonathlete and athlete. The technique will be used

to characterize the changes which occur with various deconditioning methods such as bedrest, chair rest, water immersion, and space flight. It will be used also to describe studies on various protective or preventive techniques which may be useful in controlling or preventing the manifestations of deconditioning seen with various experimental circumstances.

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